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ESTERASES IN CUTANEOUS GRANULOMATA.

G. C. WELLS.

Senior Lecturer, Institute of Dermatology,
British Postgraduate Medical Federation, University of London.

CERTAIN histochemical procedures have received a measure of acceptance as a means of demonstrating hydrolysing enzymes in tissue sections, since Gomori (1939) and Tagamatsu (1939) introduced a method for alkaline phosphatase, and since Menten *et al.* (1944) adapted azo-coupling techniques to histochemistry.

The distribution of particular enzymes in *normal human skin* has been described as follows :

- (i) Alkaline phosphatase by Fisher and Glick (1947) and by Kopf (1957) ;
- (ii) Acid phosphatase by Moretti and Mescon (1956) ;
- (iii) Simple (non-specific) esterases by Findlay (1955) and by Montagna (1955) ;
- (iv) Acetyl-cholinesterases by Hurley *et al.* (1953), by Hellman (1955) and by Becket *et al.* (1956).

Grogg and Pearse (1952) studied these enzymes in experimental tuberculosis of different organs in various laboratory animals and suggested a relationship between certain of these enzymes and tissue defence. It was therefore decided to study lupus vulgaris from the point of view of phosphatase and simple esterase content, and, during the course of this work, other cutaneous granulomata and many unrelated skin lesions have been examined in order to gain perspective.

METHOD.

Skin biopsies were made after infiltration of the area with $\frac{1}{2}\%$ xylocaine. Specimens were placed in chilled neutral 10% formol saline and fixed in the ice box (4° C.) for from 17 to 24 hours.

Sections (approximately 10 μ thick) were made on the freezing microtome, floated out on water, mounted on glass slides, and dried for a few hours at room temperature. Where possible sections of different lesions and of normal skin were mounted on the same slide so as to allow direct comparison after enzyme studies. Slides stored in the ice box preserved enzyme activity for many weeks.

MATERIAL.

The following biopsy material was used for enzyme study (numerals indicate numbers of cases studied) :

Group A.

- (i) Normal skin from various parts of the body.
- (ii) *Lesions with Mainly Lymphocytic Dermal Infiltrate.*
 - Eczema (1).
 - Banal perivascular infiltrate (5).
 - Chronic discoid lupus erythematosus (6).
 - Lichen planus (2).
 - Capillaritis (2).
 - Acne vulgaris (2).
- (iii) *Lesions with Lymphocytic and Plasma Cell Infiltrates.*
 - Late secondary syphilide (1).
 - Superficial basal cell epithelioma (1).
- (iv) *Lesions with Increase of Mast Cells.*
 - Urticaria pigmentosa (2).
- (v) *Increase in Muscle, Connective Tissue or Schwannian Elements.*
 - Leiomyoma cutis (1).
 - Fibroma durum (2).
 - Neurofibroma (1).
 - Cellular naevi (3).
- (vi) *Blistering Conditions.*
 - Pemphigus vulgaris (1).
 - Simple blister (1).

In Group A there was no increase of esterase compared with normal skin.

Group B.

With Some Simple Hyperplasia.

- Lichenified eczema (2).
- Acne keloid (1).
- Warty hyperplasia (1).
- Hypertrophic lichen planus (1).

In group B there was some increase in esterase content of histiocytes.

Group C.

Chronic Granulomata.

- Lupus vulgaris (8).
- Tuberculide (Acanthosis) (1).
- Leprosy (6, of which 4 were lepromatous).
- Sarcoidosis (3).
- Granuloma annulare (9).
- Necrobiosis lipoidica diabetorum (1).
- Early histiocytoma (1).
- Giant cell tumour of tendon sheath (1).
- Xanthoma (2).
- Lichen nitidus (1).

In group C there was great increase of esterase activity in macrophages.

ENZYMATIC METHODS.

For Alkaline Phosphatase.

(a) The Gomori calcium-cobalt method, with substrate sodium β -glyceryl mono-phosphate, was used according to the details given by Gomori (1952) and by Pearse (1953).

(b) The coupling azo-dye method of Gomori (1951) was used with α -naphthyl phosphate as substrate, according to the modification of Pearse (1953).

Comparable results were obtained with these methods but (b) was used routinely, with a trace of magnesium sulphate added to the incubating medium.

For Acid Phosphatase.

(a) The Gomori method was used with substrate β -glyceryl monophosphate in the presence of lead nitrate (Gomori, 1952).

(b) The coupling azo-dye method of Seligman and Manheimer (1949) was used with substrate α -naphthyl phosphate according to the modifications of Pearse (1953) and of Burton (1954).

Localization of acid phosphatase was not good with either method. With (a) there was a tendency for false localization in nuclei, and with the azo-dye method cytological detail was blurred. The method of Pearse was used routinely.

For Non-specific Esterases.

(a) *α -Naphthyl acetate.*—The method of Gomori (1952) with substrate α -naphthyl acetate was used, and the modifications of it detailed by Pearse (1953) and by Burstone (1956). The latter method was used routinely with Gomori's tris-hydroxyl methyl-aminomethane buffer.

(b) *Naphthol AS acetate.*—The acetate of 2-hydroxy 3-naphthoic acid anilide was synthesized according to the instructions given by Pearse (1953). The methods of Pearse (1953) and of Burstone (1956) were used and gave comparable results, but the method of Gomori (1952) was used routinely, with buffer of tris-hydroxyl methyl-aminomethane. A recent modification suggested by Holt (1956) has given the best results with clearest cytological detail.

(c) *Indoxyl acetate.*—O-acetyl 5-bromoindoxyl was used as substrate. The indoxyl acetate method of Holt (1952) was used with potassium ferro-ferricyanide as oxidizing catalyst, according to details given by Pearse (1953). This method has given good results comparable in esterase distribution and in precision with (b).

Controls and Inhibitors.

Controls—(i) A control section was routinely incubated in buffer from which the ester substrate was omitted, in order to neutralize by comparison any non-enzymatic background staining effect.

(ii) Comparison was also made with sections that had been exposed to buffer solution containing an inhibitor of reliable potency (see below).

(iii) Direct comparison of sections from several different biopsies could be made when these were mounted on the same slide, and where possible a section of normal skin was included.

Inhibitors for Simple Esterases.

The mounted sections were soaked for an hour in the tris-hydroxy methylamino-methane buffer to which the inhibitor had been added (with silver nitrate distilled water was used). The slides were then washed and transferred to the incubating mixture containing the ester substrate together with inhibitor, if this was reversible inhibitor. Controls were carried through omitting inhibitors. Results of these studies are recorded in Table I.

RESULTS.

Alkaline phosphatase.—In these sections from skin biopsies alkaline phosphatase activity could be seen at the sites described by previous workers for normal skin (Fisher and Glick, 1947). Strong alkaline phosphatase action was noted in the linings of skin capillaries. In sections having growing hairs there was seen to be strong activity in the stroma of the hair papillae (Fig. 1). Variable activity was noted in the sweat glands. Alkaline phosphatase was not detected in the granulomata studied, and in the more avascular tuberculous lesions it was conspicuous by its absence, in contrast with the capillary pattern of the normal skin. In the surrounding connective tissue there was increase of alkaline phosphatase only in relation to scarring, i.e. in fibrocytes and young connective tissue fibres.

Acid phosphatase.—It has been difficult to interpret results with the methods so far used for acid phosphatase, since the localization has been poor both with the α -naphthyl phosphate azo-coupling method and with the glyceryl phosphate method. Acid phosphatase is consistently present in all the epithelial structures of the skin, with some intensification of concentration at the keratogenous zones; this is in agreement with the findings of Moretti and Mescon (1956). In tuberculoid infiltrates acid phosphatase was diffusely present with somewhat greater concentration in giant-cell and epithelioid-cell masses, but was also present in lymphocytic masses. In Fig. 2 acid phosphatase is to be seen in the infiltrate of lupus vulgaris as well as in the normal epithelium. Acid phosphatase is also present in a variety of infiltrates unrelated to infection.

With the α -naphthyl phosphate method non-enzymatic naphthol staining was liable to occur in structures rich in lipids such as the giant-cell tumour of tendon sheath. Acid phosphatase was completely inhibited by addition of sodium fluoride (10^{-3} M) to the incubating mixture.

Simple (non-specific) esterases.—The appearance of esterase activity in normal skin varies with the ester used as substrate. α -Naphthyl acetate is rapidly hydrolyzed and there is a tendency for false naphthol staining to occur, especially in relation to lipid-rich areas and to keratin. With naphthol AS acetate localization was more precise, and with Holt's modification (1956) the cytoplasmic distribution of esterase was particularly well seen and the deposit of dye was finest. Using the entirely different principle of indigo formation with the indoxyl acetate method of Holt an identical picture was obtained. Results have been largely confined to observations with naphthol AS acetate and indoxyl acetate methods, in order to avoid the very widespread reactivity and possible false localization of the α -naphthyl acetate methods.

With the methods of Holt there appeared to be no simple esterase activity in the normal epidermis and its keratin layer except at the mouths of some



FIG. 1.—Alkaline phosphatase in normal skin. α -Naphthyl phosphate substrate with O-dianisidine diazotate. No counterstain. $\times 95$. Alkaline phosphatase activity is seen in capillary walls and in the papillary stroma of a growing hair.

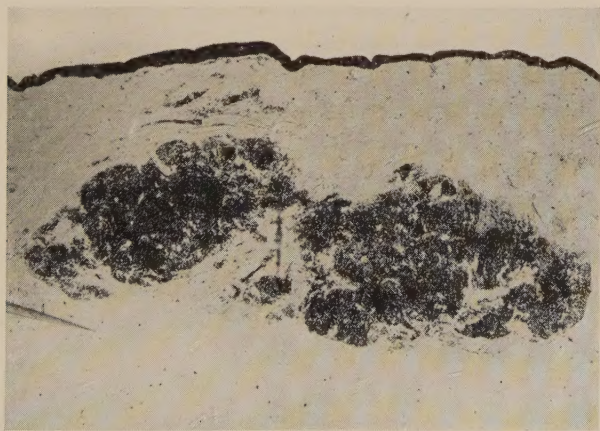


FIG. 2.—Acid phosphatase in lupus vulgaris. Glycerol β -phosphate substrate in the presence of lead ions (Lead sulphide method of Gomori). $\times 20$. Acid phosphatase is strongly shown throughout the lupus nodules and in the epithelium.

pilo-sebaceous follicles and in the intra-epidermal portions of some sweat ducts. Some acinar cells of sweat glands showed strong esterase activity, in contrast with adjacent acinar cells or other sweat glands, which might be negative. Sweat ducts contained a variable amount of this esterase in their lumina. The heaviest concentration of this non-specific esterase in normal skin was found in the pilosebaceous follicles at the point where the sebum enters the hair shaft canal (Fig. 3). In frozen sections esterase-negative yellowish sebum could often be seen at this point close to esterase-positive material which seems to be derived from the lining of the sebaceous gland duct. Sometimes esterase-positive material could be traced up the hair canal to the surface. It should be noted that not all follicles show this esterase-positive zone, and this zone is often sharply limited to the sebaceous gland canal. The sebaceous glands themselves appear to be esterase-negative though with the more unstable substrates false localization of esterase is often seen in them.

The most consistently esterase-positive elements of the skin are the scattered dendritic cells of the dermis. These cells are fairly evenly distributed throughout the dermis but they are most numerous in the *pars papillaris*. They show up by virtue of long trailing and branching cytoplasmic processes containing irregular amounts and arrangements of esterase (sometimes diffuse and sometimes granular dye deposits). For convenience I shall refer to these cells as histiocytes (while allowing that their phagocytic and wandering potentialities are not proven, and that more than one cell type may be included under this heading). These histiocytes become more prominent through increase of their esterase content in a number of chronic inflammatory conditions (Group B) such as lichenification, warty hyperplasia and acne keloid, and they may stand out very clearly in the papillae. They may be displaced by old scarring, fibroma, or leiomyoma, and may appear crowded in the normal connective tissue at the margins of such lesions. It is not clear what relationship these histiocytes of normal dermis have to the macrophages of the chronic granulomata with their far greater esterase content. Not all macrophages are esterase-positive for dermal melanophores often appear to contain no esterase.

There were remarkable accumulations of non-specific esterase in many of the granulomata studied (Group C). This strong esterase is to be seen in the cytoplasm of giant cells and in other large branched cells of the infiltrate. In lupus vulgaris (Fig. 4) these cells contrast with the epithelioid cells which are usually devoid of esterase and with surrounding lymphocytes or plasma cells which are entirely negative.

The heaviest concentration of esterase found in the material studied was in lepromatous leprosy. Here all the Virchow cells containing many acid fast bacilli had very strongly esterase-positive cytoplasm (Fig. 5). In old (long-treated) leproma, the globi show strong esterase-positive effect in their walls

(Fig. 6). In tuberculoid leprosy (Fig. 7) the distribution of esterase-positive cells was very similar to that in lupus vulgaris. That the esterase effect was produced by the cells rather than by the bacilli was suggested by the fact that a smear of tubercle bacilli from a fresh culture on a glass slide in formalin

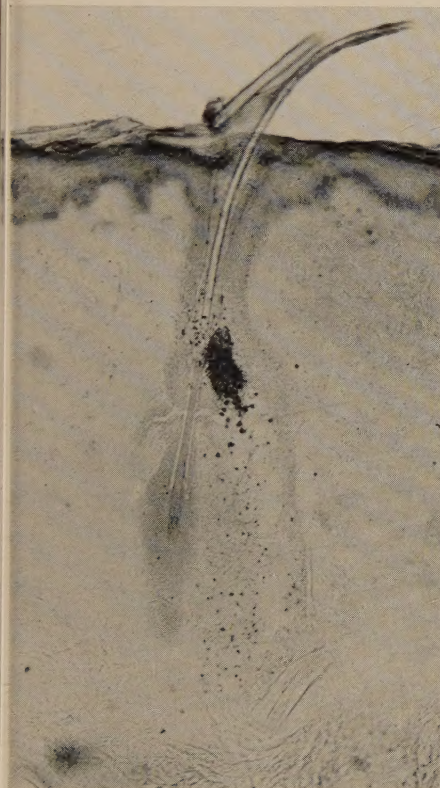


FIG. 3.

FIG. 3.—Simple esterase in normal pilosebaceous follicle. O-acetyl-5-bromo indoxyl substrate. Counter-stained with eosin. $\times 120$. There is a plug of esterase-positive material where the sebum enters the hair canal. The sebaceous gland can be faintly seen alongside the hair root. The epithelium is lightly stained with eosin.

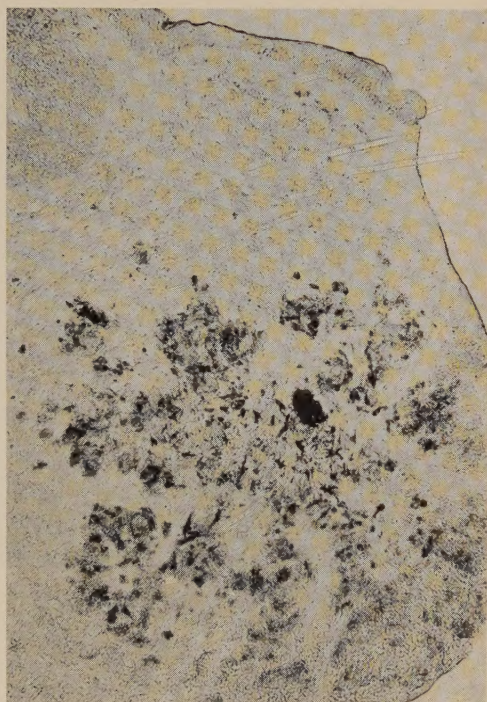


FIG. 4.

FIG. 4.—Simple esterase in lupus vulgaris. Naphthol AS acetate substrate with O-aminoazo toluene. No counterstain. $\times 20$. Esterase strongly shown in giant cells and in dendritic phagocytes. It is not seen in epithelioid cells, lymphocytes or plasma cells.

vapour and subsequently incubated in the ester substrates, produced no hydrolysis.

In acnitis the tuberculoid foci contained esterase-positive giant cells and macrophages. In sarcoidosis strong esterase activity was seen in giant cells scattered among islands of epithelioid cell infiltrate which were themselves esterase-negative. In granuloma annulare intense esterase activity was seen

in the large straggly cells which form a palisade around the degenerate connective tissue (Fig. 8). In that type of granuloma annulare in which giant cells accumulate around the superficial cutaneous blood vessels, esterase activity was related to the giant cells (Fig. 9). In necrobiosis lipoidica diabetorum esterase-positive giant cells were seen, and there were some esterase-positive cells arranged more diffusely which, in shape, were indistinguishable from



FIG. 5.—Simple esterase in leprosy. Naphthol AS acetate substrate with O-aminoazo toluene. No counterstain. $\times 33$. Esterase very strongly shown in lepra cells.

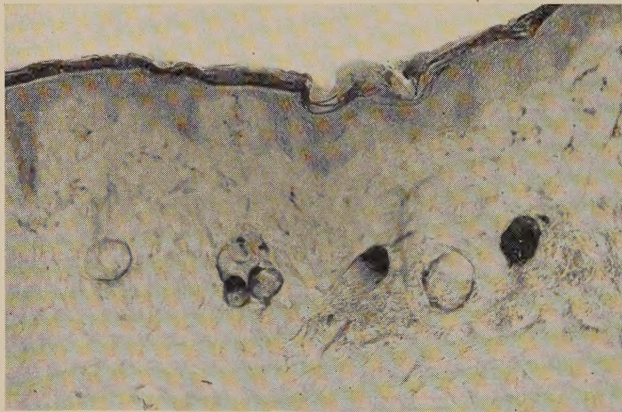


FIG. 6.—Simple esterase in globi of old treated leprosy (leprosy). O-acetyl-5-bromo indoxyl substrate, counterstained with eosin. $\times 107$. Esterase strongly shown in walls of globi containing degenerate lepra bacilli.

adjacent esterase-negative fibroblasts. In the minute granulomatous papules of lichen nitidus, a few large esterase-positive cells were seen.

Many cutaneous lesions studied (Group A) including those with lymphocytic and plasma-cell infiltrates showed no increase of simple esterase.

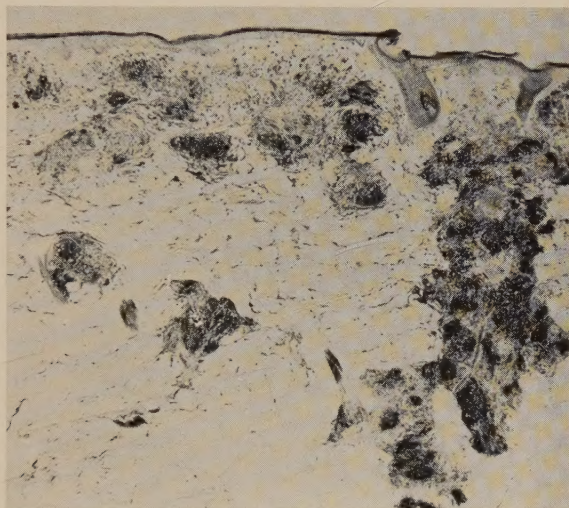


FIG. 7.—Simple esterase in tuberculoid leprosy. α -Naphthyl acetate substrate with O-dianisidine diazotate. No counterstain. $\times 30$. Strong esterase activity in giant cell foci. Darkening of the epithelium and keratin is a background effect.

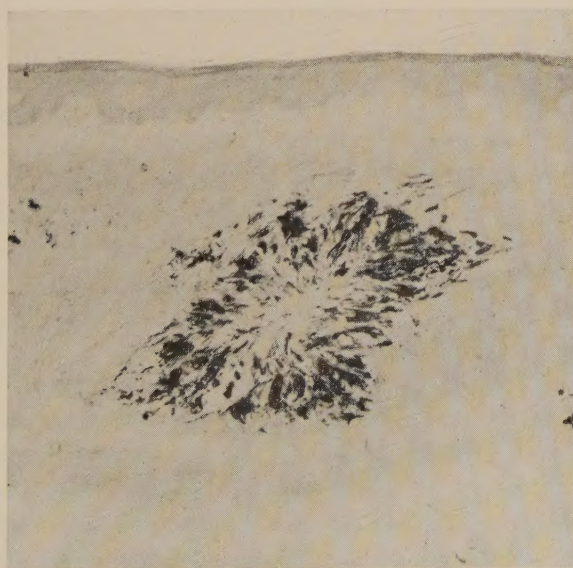


FIG. 8.—Simple esterase in granuloma annulare. α -Naphthyl acetate substrate in the presence of O-dianisidine diazotate. No counterstain. $\times 80$. Foci of connective-tissue degeneration are surrounded by large dendritic esterase-positive phagocytes.

Large esterase-positive cells are of course to be found in other tissues besides skin. They were prominent in the giant-cell tumour of tendon sheath, for example. Freshly excised human lung (pulmonary tuberculosis) was found to have strongly positive cells (alveolar phagocytes) in inflammatory areas.

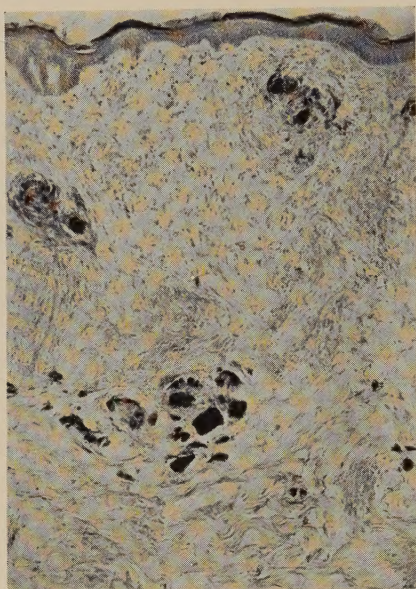


FIG. 9.—Simple esterase in granuloma annulare. O-acetyl-5-bromo indoxyl substrate, counterstained with eosin. $\times 66$. Esterase-positive giant cells are seen round small blood vessels. The epithelium is darkened by counterstain.

DISCUSSION.

Alkaline phosphatase did not appear to be increased in the granulomata studied unless there was proliferation of connective tissue or scarring. Klingmüller (1953) described increase of alkaline phosphatase in the cellular infiltrates of lupus vulgaris and of leprosy, and Kopf (1957) noted alkaline phosphatase in the lymphocytic infiltrate of lupus vulgaris. These workers relied on Gomori's method which is liable to give some false localization unless carefully controlled, and I have placed more reliance on the azo-coupling method, with which it seems that any increase of alkaline phosphatase is related to healing around the tubercles, rather than to the tubercles themselves.

Acid phosphatase is present in all the epithelial structures of the skin and in most cellular infiltrates. Grogg and Pearse (1953) showed a particular increase of acid phosphatase in the lesions of experimental tuberculosis of various laboratory animals, and suggested a relationship between this acid phosphatase and tissue defence against tuberculosis in different organs and species. While confirming the presence of acid phosphatase in tuberculoid infiltrates of skin

with some emphasis on giant-cell systems, I have been unable to relate this to specific infective processes, as similar accumulations of acid phosphatase may be found in a variety of non-infective infiltrates.

This work is mainly concerned with the simple (non-specific) esterases of skin. Moderate esterase activity is usually demonstrable histochemically in scattered cells (histiocytes) of the normal dermis, and long cytoplasmic processes show up by virtue of their esterase content. These cells are rather more numerous in the pars papillaris of the skin and they are more prominent in some hyperplastic conditions listed in Group B. Findlay (1955) described these cells but was unable to say exactly what they were. Some of them have the appearance of fibroblasts and others might be Schwannian cells or other kinds of phagocyte.

The presence of strong esterase activity in the pilosebaceous follicle at the point where sebum is discharged into the hair canal is in general agreement with the findings of Findlay (1955) and of Montagna (1955). With the substituted indoxyl method of Holt the focal accumulation of esterase in the sebaceous canal is very clear. The esterase often continues up around the hair shaft and may be demonstrable locally on the skin surface. The site of this esterase might suggest a lipolytic function, but so far no evidence of true lipase actions has been forthcoming. Simple esterase was demonstrable in some sweat ducts as well as in some of the acinar cells of sweat glands, in agreement with the findings of Findlay (1955) and of Montagna (1955).

The remarkable concentration of non-specific esterase in the giant cells and large phagocytes of chronic granulomata due to tuberculosis and leprosy suggested at first a relationship to the infection organism. The esterase might be one of the means whereby the bacillus is attacked, and its function might be the attempted hydrolysis of the lipid envelope of the bacillus. Gerstl and Tennant (1942) showed that both a lecithinase and a phosphatase were factors in the breakdown of tuberculophosphatide by the tissues.

Against this suggestion of a specific relationship between esterase cells and the infecting organism must be set the similar picture to be seen in sarcoidosis of skin. Here the presence of micro-organisms is unlikely, yet the same esterase-containing macrophages and giant cells are to be seen. Infection is even less likely to play a part in granuloma annulare, yet here too there are impressive collections of esterase (Figs. 6 and 7), and the same is true of necrobiosis lipidica diabetorum. Strong esterase activity appears to be common to many phagocytes, and was seen for example in alveolar phagocytes some of which were also laden with carbon. Steigleder and Schultis (1957) have recently drawn attention to the esterase content of cutaneous connective tissue, including some of the pathological conditions described above.

Inhibitor studies were carried out with the intention of characterizing the main enzyme or enzymes producing hydrolysis of the simple esters used

TABLE I.—*Inhibitor Studies with Simple Esterases.*

Inhibitor.	Final concentration	Per cent. inhibition of esterase
Di-isopropyl fluoro-phosphate	10^{-6} M .	75–100*
Silver nitrate	2×10^{-3} M .	75–100*
Sodium fluoride	10^{-3} M .	0–30
Sodium taurocholate	10^{-3} M .	0–30†
Sodium dodecyl sulphate	10^{-3} M .	0–30†
Eserine sulphate	10^{-3} M .	0–30
Lysergic acid	3×10^{-6} M .	0–30
Hydrocinnamic acid	10^{-3} M .	0
Hydroxylamine	10^{-3} M .	0

* Irreversible inhibition.

† Blurring of dye picture, probably through surface active effect.

histochemically (Table I). Di-isopropyl fluorophosphate and silver nitrate, in great dilution, produced strong and irreversible inhibition of this dermal esterase. This inhibition, however, does not distinguish between a variety of esterases on the one hand, and on the other hand proteases such as trypsin and chymotrypsin which are capable of hydrolysing esters. Some peptidases such as aminopeptidase would not be inhibited (Burstone and Folk, 1957) so strongly by DFP, and the lack of any effect of hydrocinnamic acid or of hydroxylamine are evidence against carboxypeptidase and aminopeptidase respectively (Pepler and Pearse, 1957). Results with sodium taurocholate and with sodium dodecyl sulphate were unsatisfactory in that dye deposition was interfered with by surface action, and there was no suggestion of activation of the esterase by these chemicals as might be expected if the enzyme were a true lipase. Only weak inhibition by eserine and by lysergic acid indicated that the esterase was neither true cholinesterase nor pseudocholinesterase.

This broad survey of hydrolyzing enzymes in cutaneous lesions draws attention away from the relationship between these enzymes and infecting organisms except in so far as the lepra cells are very rich in non-specific esterase. Instead, attention is focussed on the histiocytes or macrophages which are seen to be heavily loaded with simple esterases in a variety of chronic infectious and non-infectious granulomata. These cells are distinct from epithelioid cells and from other cells of chronic inflammatory infiltrates, and when histochemical methods for esterases have been used, their morphology is clear. It is not yet known what chemical part these histiocytes play in the metabolism of foreign material or of damaged tissue.

SUMMARY

Specimens of normal and of pathological human skin were examined histochemically for alkaline phosphatase, acid phosphatase and simple esterases.

Alkaline phosphatase was demonstrable in capillary walls, in the papillae of growing hairs and in young scar tissue.

Acid phosphatase was present in all epithelial structures and in nearly all cellular infiltrates.

Simple esterase was present in scattered dendritic cells (histiocytes) of the normal dermis. Strong esterase activity was noted in the sebaceous canal of many hair follicles, and in a few acinar cells of some sweat glands and in some sweat ducts.

In chronic cutaneous granulomata macrophages and giant cells were shown to be rich in simple esterase whereas epithelioid cells, plasma cells and lymphocytes were negative. Lepra cells were very strongly esterase-positive.

Studies with chemical inhibitors leave some doubt as to whether these simple esterases are mainly concerned with protein or lipid turnover.

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HIDRADENOID VESTIBULOACANTHOMA.

J. L. S. SMITH, M.D.(Cantab.), D.O.M.S.

Lecturer in Ophthalmic Pathology, University of Manchester.

AND

J. G. COBURN, M.D.(Manch.)

Dermatologist, Manchester and Salford Hospital for Skin Diseases,
Assistant Lecturer in Dermatological Histopathology, University of Manchester.

MALIGNANT NEOPLASIA OF EXTRA-APOCRINE SITES.

THE benign members of this group were discussed in a recent paper (Smith and Coburn, 1957).

It was pointed out that during phylogeny, mainly in primates, the vast majority of sweat glands had become divorced from the follicles. This course of events is mirrored in human ontogeny in that numbers of sweat glands whose ultimate form and function are eccrine take their origin from follicular vestibules. Later in life, this same process is again manifest in the formation of hidradenoid vestibuloacanthomata whose sudoriferous differentiation is not apocrine but eccrine in character. In such tumours the matrix cells may resemble those of the normal vestibule, being epidermal in type (vestibulo-adnexal series); alternatively, they are of a non-vestibular type, and are then more akin to those of the follicular primordial zones (adnexal series).

Benign hidradenoid vestibuloacanthomata have strict homologues among the skin cancers. In early and pre-invasive stages the true nature of some of these cancers may not be apparent, especially in the "intra-epidermal" type. In the malignant, as in the benign categories, one can recognize an *overt class* with widespread sudoriferous metaplasia and an *imperfect class* with a mainly non-specific vestibular character.

OVERT HIDRADENOID CLASS.

According to matrix type we recognize a vestibulo-adnexal and an adnexal series.

Vestibulo-adnexal Series.

There is peripheral acanthosis in which the cells as a rule show little deviation from the normal though there is hyperkeratosis. In this border zone the thickening of the rete is maximal at its junction with the main tumour and fades off laterally into a normal epidermis.

Centrally, a compact tumour develops composed of closely packed columns of downgrowing epithelium (Fig. 1). The centres of the columns are occupied

by large cells of squamous pattern ; some are individually hyalinized and others form small groups of concentrically arranged cornifying elements. There is a definitive basal layer ; between it and the central cell masses extensive spaces are seen in which lie the basophilic remains of necrotic cells. In places the epithelial columns and their contained spaces are narrow and duct-like, though their lining epithelia are almost always defective, as judged by the morphology of individual cells ; exceptions, however, occur, mainly in the less aggressive neoplasms. Near the surface are accumulations of keratin which are ultimately cast off so that the cancer cells may extend freely to the surface.

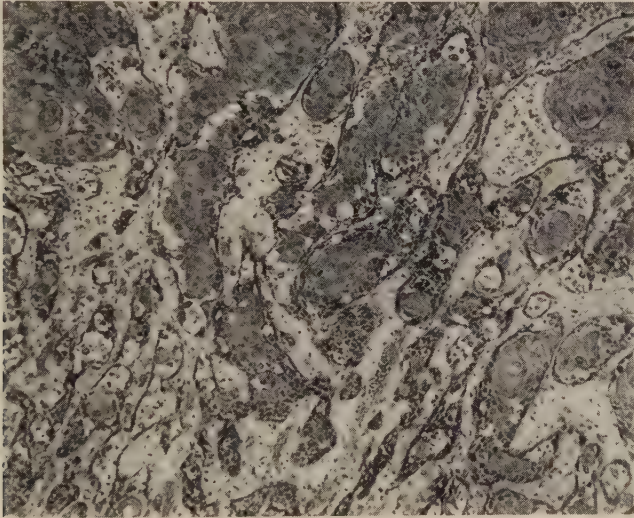


FIG. 1.—Vestibulo-adnexal matrix. Invasive columns containing duct-like spaces and squamous cell centres. Definitive basal layer. Finger. $\times 63$.

Interpretation.—The general structure duplicates that of the benign homologue. In both there is a central mass of invasive epithelium showing vestibular and sudoriferous differentiation ; the former is represented by pearls and strands of keratinizing squamous cells and the latter by ill-formed tubular lumina. The *immature* matrix cells preserve in large measure their epidermal (i.e. vestibular) patterns as manifest by their even spacing and retention of intercellular bridges. However, the tendency is for the cells to mature rapidly and many of the larger “squamous” cells seen in the basal layer may be regarded as the equivalent of duct-lining cells ; they lack the cohesion provided by true prickle systems. This and cell necrosis may lead to widespread supra-basal splitting, sometimes marked in the border zone.

Clinically the cancers are distinguished by a greater modification of the surface scale ; its verrucosity is superseded by crusts and areas resembling granulation tissue.

To such cancers Lever (1947) applies the name "adenoacanthoma" and gives their chief sites as the face and the ear, especially the latter. Many squamous epitheliomata show tubular differentiation on a small scale, and it would seem more likely that the adenoacanthoma is simply the better differentiated member of a much larger group. The tumour illustrated in Fig. 1 came from the finger. However, the best differentiated tumour which we possess came from the sole. One might well expect sudoriferous differentiation to be above average in tumours of the hairless areas of the palms and soles; the same will apply, though to less degree, where the pilo-sebaceous appendages are small or insignificant as on the auricles.

No sharp dividing line can be drawn between benign and malignant neoplasms of this series. The second example of an adenoacanthoma reported by Wansker, Smith and Olansky (1957) might well fall in an intermediate category. The histology of this papillomatous tumour from the preauricular region shows a relative excess of small, rather uniform matrix cells.

Adnexal Series.

The matrices lose their vestibular character. In the smaller matrix cells this changeover is expressed in a less regular spacing, in a marked tendency to cell individuation and in the appearance of basocellular elements. Cell maturation is much more variable and includes the production of aggregates of cells with pale cytoplasm.

Again the two main structural types are apparent: suborganoid and organoid.

(a) Suborganoid.

These are compact tumours whose overall structure, at least in the earliest stages, corresponds to that of the vestibulo-adnexal cancers. As in the benign homologues three morphological sub-types can be recognized, expressing three different modes of evolution.

Sub-type 1: The peripheral rete shows the usual acanthosis and hyperkeratosis. Over the central tumour mass the surface is at first verrucose but later becomes crusted and abraded.

Mainly in the upper zones masses of squamous epithelium surround horny material. Elsewhere the matrix cells are more protean, often forming sheets of individuated cells of varying eosinophilia, sometimes basocellular with scanty cytoplasm and crowded nuclei. Anisocytosis is often considerable, many nuclei being large and hyperchromatic (Fig. 2). Scattered areas of clear-cell epithelium are common. Spaces, usually of medium size, are evident, containing necrotic material or small groups of vacuolated cells; some of these spaces are lined by epithelium of ductular or glandular type. Towards the underside of the tumour the epithelium tends to be less solid and may be arranged in narrow strands.

Interpretation.—The theoretical importance of this sub-type hinges on the delay in the appearance of the adnexal matrices. The cancer is launched into the dermis as a simple vestibulo-acanthoma; much of its epithelium may be of relatively pale (deeper) vestibular type.

Malignancy is indicated on structural as well as on cytological grounds since the adoption of the adnexal matrix is more haphazard than in the benign homologue. Thus a squamous character is often retained in the deeper regions, though this may be in part attributable to a reversion to a vestibular form of

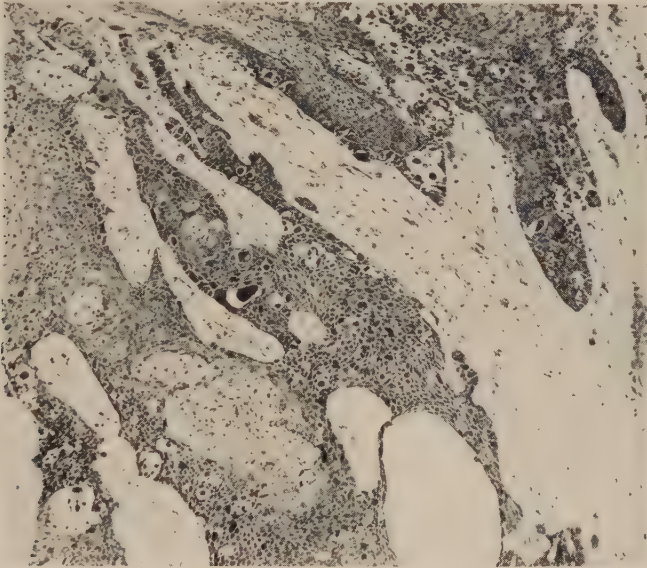


FIG. 2.—Adnexal matrix. Individuated eosinophilic cells of pleomorphic type. Limited structural differentiation. Cleft between first and second toes. $\times 72$.

cell maturation. As a consequence the distinction from the vestibulo-adnexal cancers is less clear-cut.

Sub-type 2: Around the main tumour is a broad acanthotic zone in which there is some disturbance of cell maturation, usually indicated by paler cells in the mid and upper rete; these are particularly striking within the granular layer.

The acanthosis is plane or nearly so, but centrally the upper layers of the epidermis are soon cast off leaving an eroded surface. Much of the matrix may be formed by pale cells with oval or spindle nuclei; at the origin of the invasive cancer from the rete spindle cells often dominate the histological picture. In places stromal elements may be intimately mingled with the matrix cells. Cellular differentiation is represented by the larger cells, often eosinophilic and individuated; the latter may be found in rows but only rarely is their arrangement recognizably ductular.

Interpretation.—In contrast to Sub-type 1, there is a rapid onset of full adnexal deviation so that the vestibular character of the early tumours is soon lost. Also, there is a tendency for the cells with eosinophilic cytoplasm to be interspersed by others with paler cytoplasm and by cells of basocellular nature. This and the adoption of spindle shapes reduces the contrast with the connective tissue cells and these may be so closely integrated with the neoplastic epithelium as to make the recognition of many smaller cancer cells difficult. Pathologists have been strangely reluctant to consider the possible sudoriferous nature of non-keratinizing and spindle-cell squamous carcinomata of the skin, although proliferations of this type are well known to occur in relation to tubular glands, as in the breast; the myoepithelial nature of these deeper tumours has been stressed, notably by Lever (1948). This author (1954) also recognizes a clear-cell myoepithelioma containing cuboidal clear cells in addition to the fusiform elements. Spindle-cell carcinomata may occur in regions where the only adnexal structures are sweat glands and in the absence of preceding irradiation, as in the sixth case mentioned by Brooks (1943) from the sole.

Sub-type 3: In this sub-type the matrices are largely undifferentiated and basocellular. The matrix cells tend to be of a transitional type, many being relatively mature with vesicular nuclei though their pale-staining cytoplasm is not usually abundant. Such a tumour showing attempts at tubular differentiation is shown in Fig. 3. The cell pleomorphism is less, large and clumping nuclei being relatively few.

Interpretation.—Conventional classification would relegate tumours of this sub-type to the intermediate variety of metatypical basal cell carcinoma (Darier and Ferrand, 1922). They cannot, however, be sharply separated by their histology or behaviour from deeply, though locally, infiltrating basaloid-mata. Several metastasizing basal-cell carcinomata have been reported though rarely has their histology been portrayed in detail. In the case of Fordyce (1902) the local recurrence was morphoeiform with a finely trabeculate structure, apparently ductular in nature. Finnerud (1924) described the histology of his second case, also a recurrence, as being of trabecular pattern with anastomoses forming acini. The illustrations of De Nevasquez's case (1941) suggest a sudoriferous nature, notably perhaps the intravascular metastasis with its rather characteristic cribriform pattern, an appearance sometimes encountered in neoplasia within the ducts of the mammary gland.

(b) *Organoid.*

We have only one florid example of this type, a tumour which was removed from the sacral region.

There is moderate acanthosis with some increase of the surface scale. The matrix cells include discrete elements, either small or with more ample and often eosinophilic cytoplasm, and masses of pale epithelium with large vesicular

nuclei in which the tendency to individuation is much less. The adnexal matrices are present over wide areas of the basal rete and in the walls of the underlying appendages; they are interrupted by areas of normal-looking epithelium. In the sweat ducts the histology is particularly striking, the cancer

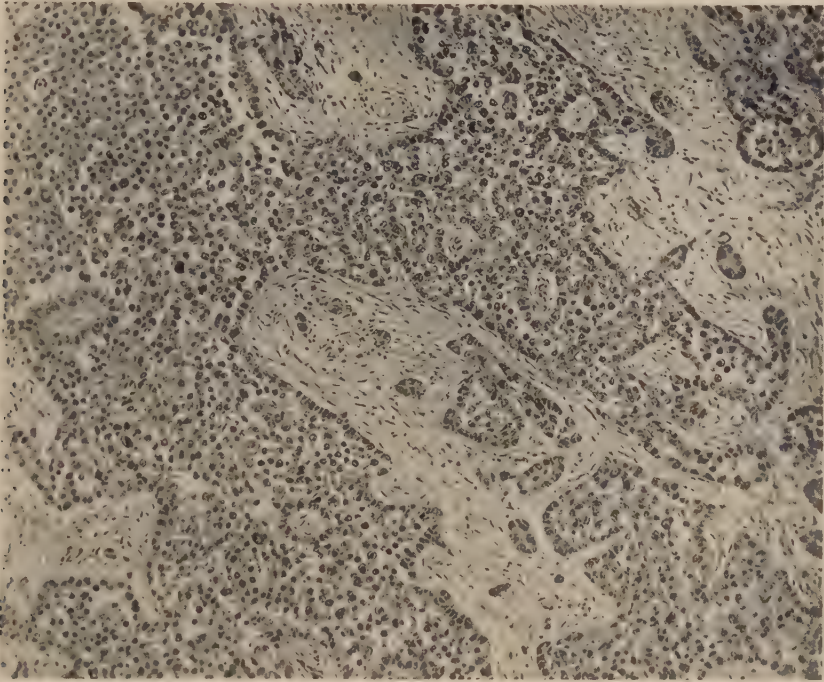


FIG. 3. Adnexal matrix of "transitional type". Imperfect tubular differentiation. Cheek. $\times 110$.

cells lying between the cuticular duct lining and the basal layer (Fig. 4). In parts of the epidermis a few single or small groups of cancer cells are evident in the mid and upper rete, being carried by the normal upward movement of the rete cells.

In places the dermis has been invaded by groups of matrix cells of a small angulated or polyhedral type.

Interpretation.—The fully developed form of this tumour, as portrayed above, must be exceedingly rare as indeed is its benign counterpart. In spite of poor structural differentiation, such neoplasms are the malignant homologues of the organoid adnexal series and must be recognized as such. The distribution and type of the cancer cells are those of Paget's disease. Not only is the above example extra-mammary but it is also extra-apocrine: the structure of the underlying sweat coils and ducts is eccrine. Similar cases are hard to find. The one reported by Louste and Rabut (1934) from the scapular region seems to be

a genuine example. Even so, one may easily overestimate the rarity of these organoid cancers. Less advanced lesions with smaller and relatively uniform matrix cells may be passed over as intraepidermal carcinoma or as basocellular cancer, while the rare exotic cases may be labelled amelanotic melanoma. Even in apocrine regions some authors have interpreted the Paget picture as malignant melanoma (Kreibich, 1911; Civatte, 1928; Drake and Whitfield, 1929) or considered this possibility (Miescher, 1929).

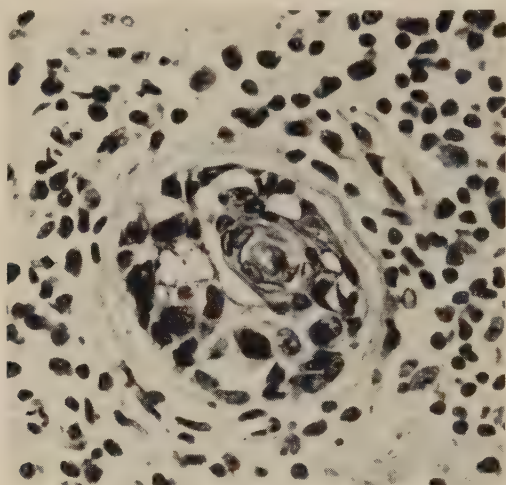


FIG. 4.—Adenocarcinoma with cancerous transformation of eccrine sweat duct. Preservation of cuticle-lined lumen. Sacrum. $\times 470$.

The unusually widespread involvement of the appendages, especially the sweat ducts, is striking. Nevertheless, in suborganoid tumours the sweat coils sometimes show a limited proliferative activity, as has been noted by Lever (1954) in his account of the adenoacanthoma.

Developmental Stages.

So far our histological analysis has been confined to well established invasive cancers, whose histological subdivisions duplicate those of benign hidradenoid vestibuloacanthoma. The general structure of their benign homologues is understandable in terms of adnexal deviation; each is basically a vestibuloacanthoma modified by adnexal matrices capable of sudoriferous differentiation, though among members of the adnexal series the vestibular phase may be transitory or minimal. The organization of the malignant tumours is less simple, since their structure also reflects the stage in development at which cancerous matrices make their appearance. We have previously suggested that malignant examples of hidroacanthoma simplex (Smith and Coburn, 1956) could be divided with advantage into consecutive and primary cancer,

the former representing the malignant transformation of a benign homologue. By applying this basic, though by no means absolute, subdivision the structural interpretation of the present group of neoplasms is simplified. In the following section the evolution of malignant hidradenoid vestibuloacanthomata will therefore be discussed as either consecutive cancer or primary cancer.

Consecutive cancer.—Here the cancer is preceded by a benign vestibuloacanthoma which may be either non-specific or hidradenoid. As a rule the advent of the cancer seems to coincide with the elaboration of the adnexal matrices proper; the matrix cells are the cancer and their junction with the benign portions of the tumour is often sharp.

In consecutive cancers belonging to the vestibulo-adnexal series and to Sub-type 1 of the adnexal series one sees the remains of the benign vestibuloacanthoma, within whose framework the malignant matrices have developed. The benign phase is often represented by actively growing "basal-cell papillomata" with their preponderance of small cells. In such neoplasms the onset of malignancy may be heralded by some upward migration of matrix cells through the rete where they contrast strongly with the surrounding squamous cells. Less commonly malignant matrices may form in papillomata of long standing. The initial lesion can be a typical seborrhoeic wart, the structural patterns of which may be freely evident outside the main tumour area. The belief that seborrhoeic warts seldom undergo malignant degeneration is true, though it only applies strictly to those warts which have become static or nearly so. A sudden renewal of growth is often indicative of malignancy in long-standing lesions. Fig. 5 illustrates such a tumour from the dorsum of the hand. The malignant matrices are of the basocellular type (? hidradenoid) and sharply delineated from the remains of the earlier papilloma.

Less commonly, cancer may supervene in established overt tumours of the adnexal series. Owing to the ephemeral nature of the initial vestibular phase in Sub-types 2 and 3, such an event constitutes a malignant transformation of previously benign matrices. In such cases the cancerous trend has probably existed since a relatively early stage, a sudden metamorphosis being unusual. Fig. 6 illustrates eccrine duct differentiation in a basocellular matrix of benign appearance. Some of the neighbouring groups of cells, however, are much more pleomorphic. In this third sub-type, the restricted cellular differentiation tends to reduce the contrast between benign and malignant matrices, though the latter always show greater cytological abnormalities.

The concept of consecutive cancer is an important aid in the elucidation of these polymorphous structural patterns.

Primary cancer.—Three important attributes of primary malignant vestibuloacanthomata are: (i) An acanthosis which is plane or relatively so, (ii) an *in situ* course which is often prolonged, (iii) a vestibular build which may be imperfectly expressed.



FIG. 5.—Consecutive cancer. Persistence of dark-staining squamous cells of initial papilloma.
× 107.

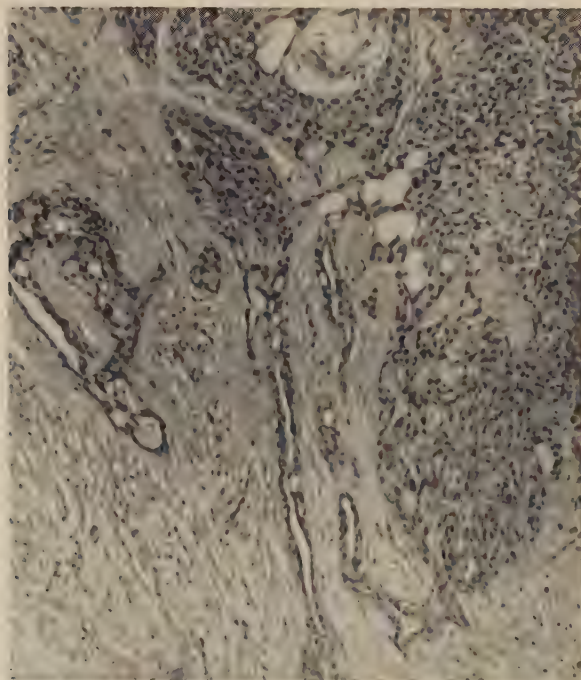


FIG. 6.—Consecutive cancer. Eccrine sweat duct differentiation in basocellular matrix. × 120

Vestibulo-adnexal series.—The senile keratoma is a clinical lesion whose histology may be very diverse. The histological picture may recall Darier's disease or may show a Bowen-like dyskeratosis, or even transitions to basal-cell epithelioma (Portugal Cline and Rocha, 1950). In primary cancers of this series the pre-invasive neoplasms are drawn from the senile keratoma group. They either are simple hyperkeratotic lesions with limited numbers of dyskeratotic cells or conform to the classical Freudenthal type (1926). Particularly in the latter form, existing follicular vestibules are plugged by horny lamellae continuous with the general surface scale; this scale also descends into the rete ridges in the form of plugs, representing an attempt to form new vestibules

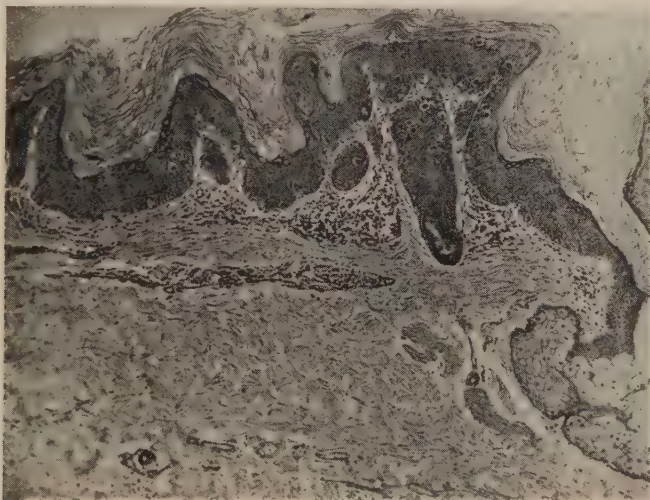


FIG. 7.—Senile keratoma. Plugging of rete ridges and follicular vestibule. $\times 63$.

(Fig. 7). Unna (1896) in his description of "sailor's skin" drew attention to the formation of "conical horny taps, like corns" associated with thinning or loss of the granular layer. In the stratum corneum are columns of parakeratotic cells, often overlying the tips of the papillae, and giving rise to the alternating hyper- and parakeratosis. The sometimes widespread suprabasal splitting of the deeper rete is to be interpreted as imperfect duct formation; occasionally well-formed duct spaces are formed. Many of the "buds" arise from existing vestibules and to a less extent from the upper parts of sweat ducts; they often form mantles, especially around the former, or sometimes a continuous swelling (Halter, 1952). These also may be partly canalized.

The cytological disorder which is present to varying degree stamps these keratomata as cancerous and if invasion of the dermis occurs the sequel is likely to be an overt hidradenoid vestibuloacanthoma. This explains the frequent co-existence of keratoma senile and adenoacanthoma, as recorded

by Lever (1947). The commonly associated seborrhoeic warts represent benign vestibuloacanthomata, usually non-specific but occasionally hidradenoid in part. The structure of the seborrhoeic wart is not fundamentally different from that of many senile keratomata. Waelsch (1905) saw no reason to separate them.

Adnexal series.—The histological picture reflects the mode of evolution of the individual neoplasm. As in the vestibulo-adnexal forms, there may be a well marked vestibular stage associated with considerable hyperkeratosis, though usually there are greater abnormalities in the maturation of the rete cells; paler cells, representing deeper vestibular epithelium, make their appearance in the mid and upper rete with some consequent reduction in the formation

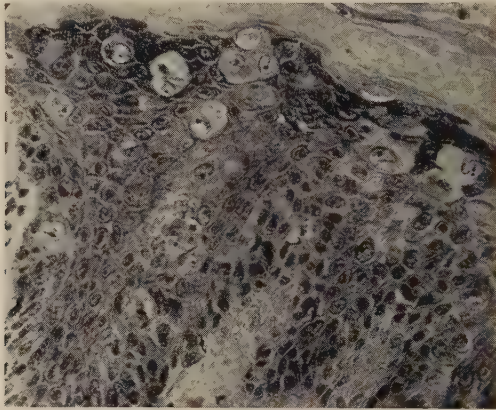


FIG. 8.—Primary cancer of adnexal series. Early vestibular stage with pale elements in the mid and upper rete. Dorsum of hand. $\times 200$.

of keratohyalin granules (Fig. 8). Even in early neoplasms there is some production of adnexal matrices leading to an abnormal arrangement of the cells in the deeper rete.

In primary, as in consecutive cancer, the vestibular stage may be short lived or poorly expressed. Such *in situ* cancers serve as a starting point for invasive tumours of Sub-types 2 and 3. Rare but striking examples exist in which the rete is largely replaced by clear-cell epithelium. The approximation of the cell borders in the deep as well as in the superficial rete produces a most characteristic picture (Fig. 9), of a type which is largely the equivalent of the early embryonic surface epithelium and which would be classified as Bowen's disease. This last tumour had become invasive in part; the invasive epithelium shows the matrix patterns of Sub-type 2 with a now much enhanced cellular pleomorphism. Other *in situ* cancers have mainly basocellular matrices, though there is always some admixture of clear cells. The case shown by Rook (1950) is of interest as it was a solitary Bowenoid cancer of the palm which had become

invasive in basocellular form. A case quoted by Jadassohn (1926) is notable in that three types of epithelial proliferation—vestibular, clear-cell and basal cell—occurred together in one lesion though affecting separate areas without the usual intermingling. Jadassohn described this neoplasm from the back of the hand as comprising a squamous epithelioma, a Bowen lesion and a basalioma with duct differentiation. When the rete is occupied by matrices of basocellular

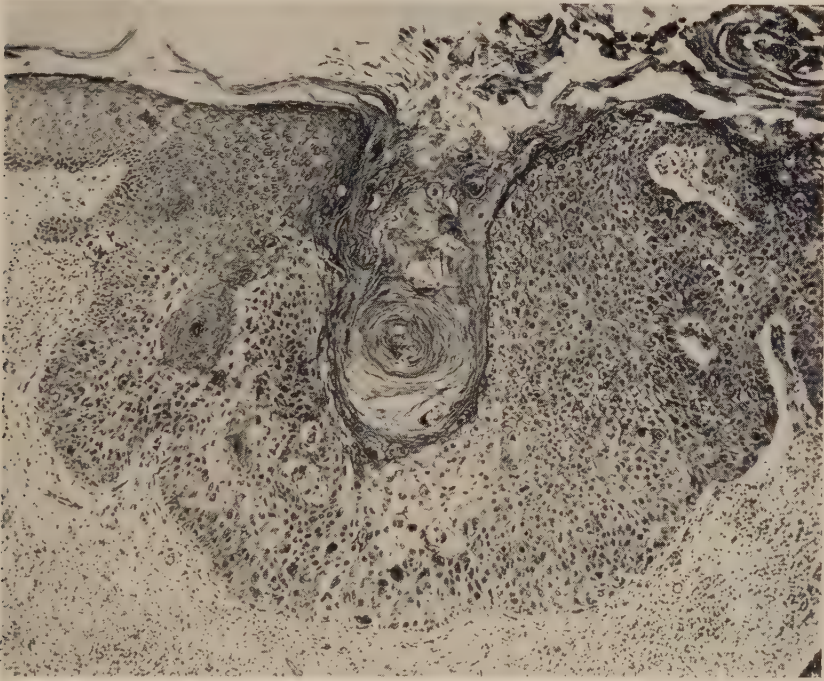


FIG. 9.—*In situ* cancer largely composed of clear-cell epithelium. $\times 95$.

pattern it is not usually possible to decide at the *in situ* stage whether the neoplasia is hidradenoid or not. Malignancy is indicated by cell pleomorphism and also sometimes by a peculiar broken appearance of the epidermis owing to the temporary survival of islands of normal squamous cells.

A few intra-epidermal carcinomata exist in which there is a moderate though extensive acanthosis with partial replacement of the deeper rete by small cells, between which a considerable loss of intercellular bridges has occurred and among which are a few larger Paget-like elements. This widespread appearance of small individuated matrix cells in the deeper rete is striking, though well exemplified in some cases of Paget's disease, both mammary and extramammary; in extra-apocrine sites such pictures are uncommon. The distribution and patterns of the matrices correspond to those of an organoid tumour of the adnexal series; the uniformity of their cells suggests a low grade of malignancy.

IMPERFECT HIDRADENOID AND NON-SPECIFIC CLASSES.

Squamous-cell epitheliomata may invade the dermis in almost pure vestibular form as closely packed columns of rounded or polyhedral shape, the centres of which are occupied by keratin masses. Such tumours have a very low grade of malignancy. In other squamous epitheliomata the disposition of the cells is more erratic, both in relation to the surrounding connective tissue and to many of their enclosed cavities. The formed elements within the latter often include individuated hyalinized cells and others with pale vacuolated cytoplasm. This altered form of cell maturation may be interpreted in a negative sense as disordered keratinization or in a positive sense as commencing adnexal deviation. The former is the generally accepted view; Willis (1948) warns against interpreting spaces within squamous cell cancers as being of glandular nature. In our opinion the modified cellular differentiation often indicates commencing sudoriferous metaplasia though the structural arrangement of the cells may not support this contention. Nevertheless, imperfectly deviated tumours can show frankly sudoriferous areas with duct differentiation. Also banal squamous epitheliomata may metastasize in adnexal form, with the production of well differentiated ducts.

We would stress that slowly growing epitheliomata often have a pronounced vestibular character. Many such vestibuloacanthomata arise in senile skin but others have a varied aetiological background, such as that provided by old inflammatory lesions. A good example of the latter is the epithelioma from the back of the hand arising on the scar of an old burn reported by Kreibich (1926). This author drew attention to the numerous comedo-like plugs which peppered the surface. The tendency for rete cells to adopt a vestibular maturation, often progressing to the formation of horny plugs, is not confined to neoplastic conditions. This feature dominates the histology of Kyrle's disease (1916), the descriptive title of which might well be modified to "vestibulokeratosis in cutem penetrans".

It is however lesions of *acute onset* which furnish the greatest difficulties in clinical assessment and histological classification. In 1936 MacCormac and Scarff introduced the molluscum sebaceum, later to be more suitably termed "keratoacanthoma"—the name adopted by Rook and Whimster (1950). The existence of such an entity was soon questioned, as by Savatard (1937) to whom the molluscum sebaceum seemed identical with the "button" epithelioma (squamous carcinoma). Beare (1953) accumulated no less than 76 cases in 38 months, as compared with double that number of squamous cell cancers. The dangers of a purely clinical diagnosis are well brought out by a case in this series which had been specially photographed as a molluscum sebaceum but which histologically proved to be an anaplastic squamous

carcinoma. These difficulties in clinical selection are explained by the basic identity of the two conditions. The true keratoacanthoma is essentially a non-specific vestibuloacanthoma which like its benign counterparts, as exemplified by seborrhoeic warts, is liable to spontaneous arrest. Progressive neoplasia beyond a few weeks, however, is strongly indicative of the presence of adnexally deviated matrices; should the latter be hidradenoid the resulting suborganoid tumours may be vestibuloadnexal or adnexal (Sub-type 1).

The keratoacanthoma presents as a raised hemispherical tumour with a central horny mass. Other forms of pseudoepitheliomatous hyperplasia are verrucose or even of a nodulo-vegetating type (Grinspan and Abulafia, 1955), the former being comparable with the verrucoma of Gougerot (1929). Nevertheless, the keratoacanthoma remains the most suspect type of pseudocarcinomatous proliferation, both clinically and histologically. Its general structure results firstly from its rapid growth, secondly from an emphasized tendency to involve the upper ends of the appendages, and thirdly from the rapid maturation of the cells leading to abundant horny material. This triad of features is harmless in the absence of adnexal deviation. Should the latter occur, however, the triad becomes more sinister since it would stamp an adnexally deviated neoplasm as truly carcinomatous.

SUMMARY.

Malignant hidradenoid vestibuloacanthomata of extra-apocrine sites are described. The early neoplasia is vestibular in character, but is modified, sooner or later, by adnexally deviated cancerous matrices of sudoriferous type. The structural range is augmented by the existence of consecutive and primary cancers. The former represent the malignant transformation of benign vestibuloacanthomata, non-specific or hidradenoid. The early stages of the latter are formed by senile keratomata and *in situ* carcinomata.

The histological subdivision, at least of invasive forms, duplicates that of the benign homologues, and individual neoplasms are allocated to the vestibulo-adnexal or to the adnexal series. Structurally differentiated examples include the adenoacanthoma which, it is suggested, represents only the better differentiated members of a much larger group, many squamous cell cancers being in fact hidradenoid including those of spindle type. The matrices may be predominantly of basocellular or intermediary type and in a few cases their arrangement is that of Paget's disease.

In non-specific vestibuloacanthomata the neoplastic process tends to become arrested. This is well illustrated by the keratoacanthoma, whose benign course can be correlated with the failure to elaborate matrices of an adnexal nature.

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A CASE OF LUPOID SYCOSIS OR ULERYTHEMA SYCOSIFORME BEGINNING IN INFANCY.

L. J. A. LOEWENTHAL, M.D., M.R.C.P., D.T.M. & H.

Dermatologist, General Hospital ;
Hon. Fellow, South African Institute for Medical Research,
Johannesburg.

IN the wider field of scarring folliculitis the problem of lupoid sycosis has frequently aroused special interest. The case reported here is unique in certain respects and emphasizes the difficulty of accepting a rigid classification for this group of cases. In particular the identity of lupoid sycosis (Milton and Brocq), ulerythema sycosiforme (Unna) and various other titles comes under review.

CASE REPORT.

An Indian male, aged 17, sought advice on 27.x.56 for extensive loss of scalp hair.

History.—At the age of 3 months he was alleged to have had varicella and immediately thereafter lesions began on the scalp. No adequate description of these lesions could be obtained, but they are said to have begun at the occipital hair margin and extended forward on either side, leaving the affected areas hairless. About 4 years ago the condition reached the temples and began to extend down the cheeks. One year ago the eyebrows began to be affected in a similar way. Pubic and axillary hair appeared 3 years ago and the beard and moustache one year ago. These areas have so far not been affected. Subjective symptoms were not a complaint.

The patient has suffered from no serious illness; his mental development, as judged by his school career, has been normal. There is no record of a similar condition affecting other members of his family.

Examination.—The patient is thin and undersized, but otherwise normally developed physically and mentally. The following cutaneous lesions are seen:

(i) The side-whisker areas show symmetrical, infiltrated, sharply outlined, scaly erythema (Fig. 1). At the margin of these areas a few pinhead-sized superficial pustules can be found; these have never exceeded 6 in number at any examination and none have been seen inside the affected areas. The eyebrows show the same infiltrated, scaly erythema and patchy loss of hair. Diascopic examination does not reveal any "apply jelly" nodules.

(ii) The sides of the neck, as far down as the clavicles, show numerous atrophic scars with white centres and pigmented margins (Fig. 2).

(iii) A large part of the scalp is atrophic, smooth and completely hairless. The affected area extends almost to the vertex at the back (Fig. 3) and forwards over the ears in bands about 2 in. deep (Fig. 1); it is sharply demarcated from the normal scalp and no inflammatory lesions are found in or near the hairless area. At the lower margin posteriorly a narrow band of hair growth is preserved; immediately above this the hairless surface, though not keloidal, is not completely smooth and presents a few, small, irregular hypertrophic scars and tiny pits. Similar pits are seen on the nose and on otherwise unaffected areas of the face. Except at the occipital marginal area the whole affected scalp is smooth and shows no vestige of follicular openings.

Laboratory investigations.—Hairs and scales from the periphery of the inflamed areas on the cheeks were negative for fungi on direct examination and culture. The contents of a minute pustule yielded a mixed growth of *Staph. aureus* and *Strep. viridans*. Both organisms showed *in vitro* sensitivity to chloramphenicol, chlortetracycline, oxytetracycline, erythromycin, tetracycline and novobiocin. The Kahn reaction of the serum was negative.



FIG. 1.



FIG. 2.

Histology.—Two 6-mm. punch biopsy specimens were removed, one from either cheek, fixed in 10% formalin and embedded in paraffin wax. Sections were stained with haematoxylin and eosin and with Weigert's elastic stain.

Biopsy 1 (27.x.56) was taken from the centre of a plaque, where there was scaling but no pustulation.

The epidermis is normal except in one area where a microscopic subcorneal abscess, consisting of polymorphonuclear leucocytes, is roofed with a parakeratotic layer. No pigment is seen in the basal layer.

The corium is oedematous and the upper two-thirds are occupied by a marked cellular infiltrate which reaches the epidermis over the greater part of the section. The superficial capillaries and lymph vessels are dilated. Very little collagen or

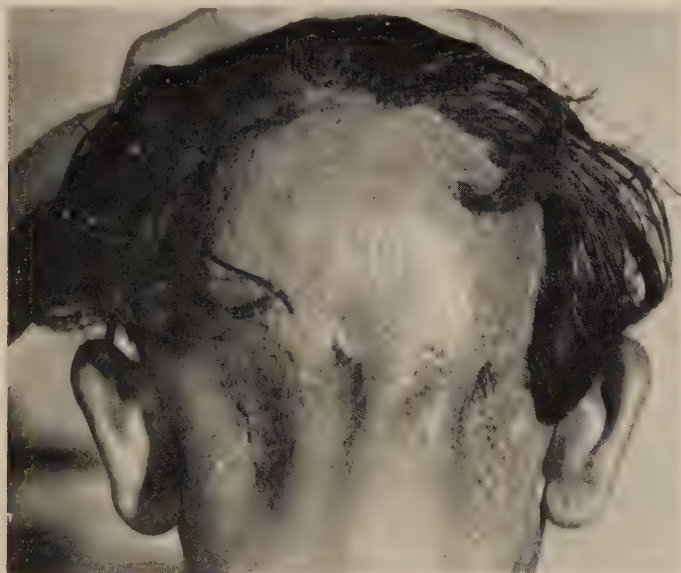


FIG. 3.

elastic tissue can be seen except at one end, where the infiltrate gives place to irregular bands and whorls of connective tissue; this has practically replaced the cellular structure of the wall of a hair follicle in the upper third of the corium, though the hair shaft is still present in the centre. The cellular infiltrate is diffuse, without any obvious tendency to be grouped around vascular or adnexal structures. It consists of lymphocytes, histiocytes, plasma cells and fibroblasts, in this order of density. Numerous dermal chromatophores are present in groups in the upper third of the corium. Normal sweat glands are present in the lower third.

Biopsy 2 (13.xii.56) was taken from the margin of a plaque and includes a minute pustule. The epidermis is irregularly acanthotic and contains a superficial abscess whose contents are exclusively polymorphonuclear leucocytes. This abscess (Fig. 4) obviously occupies the ostium of a hair follicle, and this is confirmed by the presence of a hair shaft among the pus cells. Around and below the abscess there is a dense mass of plasma cells among which are a few multinucleated giant cells of the foreign body type. This plasmoma sends diffuse and perivascular extensions throughout the corium, whose structure shows separation by oedema and fragmentation. In the lower dermis several hair follicles are infiltrated by lymphocytes, histiocytes and

multinucleated giant cells (Fig. 5) and some are surrounded by a cellular infiltrate in which plasma cells are predominant.

Sections stained by the periodic acid-Schiff method showed no fungal elements; Gram's stain revealed several groups of Gram-positive cocci resembling staphylococci in the abscess.



FIG. 4.

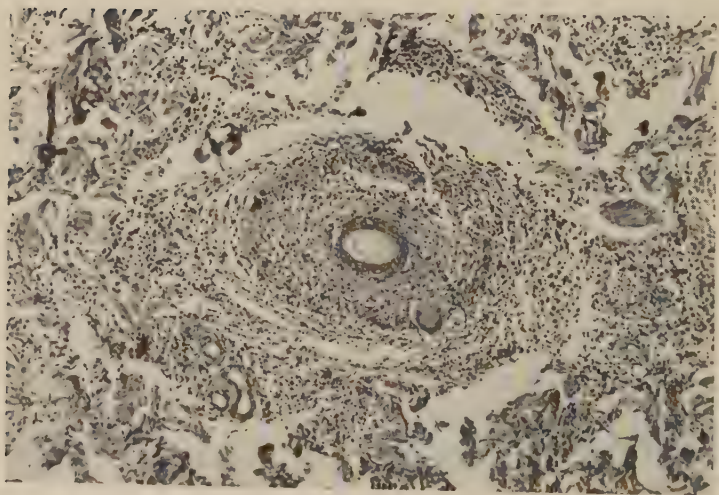


FIG. 5.

Summary of Histological Findings.

Biopsy 2, from the edge of a lesion, represents the earlier stage. The whole corium and especially the hair follicles is the site of a torpid and in places granulomatous inflammatory process: the usual reaction to pyococcal infection is seen only in the ostium of a hair follicle. In Biopsy 1 the infiltrate has thinned out and includes far fewer plasma cells, while early fibrosis, especially around a hair follicle, has appeared. Again the polymorphonuclear reaction is superficial, being represented only by a

subcorneal micro-abscess. This contrast—superficial suppuration and a deeper plasmoma—is stressed by Vilanova and Gallego (1946) in their first case.

Progress.—Oxytetracycline (terramycin) was given in doses of 250 mg. *q.i.d.* for 2 weeks. At the end of this course all redness, scaling and infiltration had disappeared. Seen 2 months later, without any further treatment, the improvement was maintained. Eighteen weeks after the end of treatment there was still no relapse but mild blepharitis was noted.

DISCUSSION.

According to Crocker (1893) and to Vilanova and Gallego (1946) the term “lupoid sycosis” was coined by Milton, in about 1860, for a chronic scarring folliculitis which begins in the side-whisker area and travels downwards on the cheeks. Crocker and several later writers assume that the same disease was described, in ignorance of Milton’s work, by Brocq (1888) as “sycosis lupoides” and by Unna (1889) as “ulerythema sycosiforme”. Vilanova and Gallego hold this assumption to be incorrect, in that Brocq’s condition is primarily a folliculitis with secondary scarring atrophy whereas Unna’s is essentially an erythema, also followed by atrophy but without folliculitis, except as a late manifestation. In Unna’s (1896*a*) own account the existence of suppurative folliculitis is categorically denied. Vilanova and Gallego stress that previous authors, while affirming the identity of these two conditions, paradoxically distinguish the two contrasting clinical pictures described above. They rightly add that the rarity of these conditions limits one’s experience and were able to describe two contrasting cases, one of which they regard as lupoid sycosis and the other as ulerythema sycosiforme. In support of their dualist concept, the following quotations are apt.

Lupoid sycosis.—(a) Darier (1928): “. . . begins in the beard, especially on the cheeks. It produces agminated follicular pustules, with inflammatory redness and diffuse, superficial infiltration of the skin.”

(b) Radcliffe-Crocker (1893): “pus infiltration is greatest at the fundus of the hair follicle.” In support of this he quotes Robinson (1877).

Ulerythema sycosiforme.—Unna (1896*a*). “The affection begins in the beard or temporal region, with flat, elevated, sharply margined erythematous spots, on which superficial vesicles, crusts and scales are formed . . . The addition of impetigo may make it appear like a coccogenic sycosis, but the atrophy of the cutis in this affection is never a result of suppuration, and the disappearance of the hair is only a manifestation of the atrophy of the whole epithelium.”

As examples of those who believed the two conditions to be identical, Vilanova and Gallego mention Ducrey and Stanziale, Arndt, Spring and Nakagawa without, however, giving precise references. A representative quotation (freely translated by the writer) is from Frieboes (1924), in the description of sycosis barbae: “. . . the flat atrophying form is identical in appearance except for the absence of a marked preceding stage of pustulation ;

particularly when it is situated on, or spreads to the lateral parts of the scalp (possibly with sparing of the lower beard area), it is unnecessarily designated *ulerythema sycosiforme*."

A painstaking attempt was made by Vilanova and Gallego to differentiate the histological characters of the two conditions. Unfortunately however the microscopic findings in their case of "lupoid sycosis" approximate closely to Unna's description of the histopathology of *ulerythema sycosiforme* and, incidentally, to the findings in Biopsy 2 of the case reported here. It will be noted, too, that considerable differences exist between the two biopsies in this case (taken within a period of 2 months), obviously reflecting different stages of the same process.

Synonyms.—Under sycosis Kaposi (1895) included Köbner's folliculitis barbae and acne mentagra. He mentioned that the eyebrows and scalp might be involved. Earlier Hebra (1868) had credited Köbner with the separation of folliculitis barbae from sycosis parasitica, though obviously suspicious of his case records. He also gave a painstaking review of such conditions as lichen menti and herpes pustulosus mentagra (Alibert) without, however, being able to do more than guess at their nature. Hallopeau and Leredde (1900) complicated matters by differentiating *folliculites cicatricielles simples de la barbe* from sycosis. Of their 6 sub-varieties *acné pileaire cicatricielle dépilante de Besnier*, which sometimes affects the scalp by direct extension, seems to be relevant to the condition under discussion. Hoffman is quoted by Vilanova and Gallego as describing folliculitis sycosiformis atrophicans capillitii and barbae as variants of the same condition. Darier (1928) gives lupoid acne "of the Americans", *ulerythema sycosiforme* and *dermite sycosiforme atrophiante* of Ducrey and Stanziale as synonyms.

The case presented here shows certain points of interest, apart from its unsolved nosological position.

Age at onset.—All accounts of lupoid sycosis and similar conditions imply, if they do not actually state, that it is a disease of the adult male. Onset in the scalp in infancy with subsequent spread to the eyebrows and side-whisker area has apparently not been reported.

The outlying scars (Fig. 2) are not mentioned in any available description of lupoid sycosis or *ulerythema sycosiforme*. Curiously enough, Unna (1896b) describes involvement of the eyebrows, scalp and neck, with scarring, in severe cases of *ulerythema ophryogenes*; superficially there is a slight clinical resemblance but closer examination and, above all, the histology prevent any confusion.

SUMMARY.

A case of progressive follicular scarring alopecia, beginning in infancy, is described. The assumed identity of lupoid sycosis and *ulerythema sycosi-*

forme is discussed but cannot be accepted or rejected on the evidence so far available.

The pathological work was done at the South African Institute for Medical Research, and the interest of the Director, Dr. E. H. Cluver, and of Dr. H. I. Lurie, is gratefully acknowledged. The photomicrographs are by Mr. M. Ulrich, of that Institute.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. LOUIS FORMAN.

21 February 1957.

Acrokeratosis Verruciformis.—Dr. ARTHUR ROOK and Dr. DANILO STEVANOVIC.

A boy aged 8, an only child born at full-term to unrelated parents. No similar condition is known in the family.

History.—Warty patches on the hands and feet were present at birth and have very slowly increased in size in proportion to general body growth. No new lesions have appeared on the limbs but about three years ago a number of small warts were noticed on the forehead and have persisted unchanged in size and number. The forma-



FIG. 1.

tion of blisters in response to trauma has not been observed. The child's health is otherwise excellent.

Examination.—The patient's general development is normal for his age; his intelligence is good. There is no abnormality of hair, teeth or nails. On the dorsal aspects of the metacarpo-phalangeal and interphalangeal joints of all fingers there are numerous flat warty papules, contiguous but discrete, forming an irregular mosaic (Fig. 1). Similar lesions are present on the flexor and medial aspects of the wrists. Irregular groups of similar papules are present on the dorsal aspects of both ankles and of the toes and over the Achilles tendons. Their distribution is less symmetrical than on the hands and the individual lesions show greater variation in size and shape and less tendency to regular grouping. Palms and soles show patchy hyperkeratosis, most conspicuous on pressure areas. The outlines of the individual papules of which the plaques are composed are well defined in some areas but indistinct in others. A few small papules resembling plane warts are present on the forehead.

Investigations.—Carotenoids: 127 $\mu\text{g.}/100$ ml. Vitamin A: 79 i.u./100 ml.

Histology.—Conspicuous hyperkeratosis and patchy parakeratosis. Moderate acanthosis and an increase in thickness of the granular layer. No vacuolation.

Comment.—The differentiation of acrokeratosis verruciformis from epidermodysplasia verruciformis is not always possible on clinical grounds alone. There are, however, certain differences. In acrokeratosis, the lesions are usually confined to the extremities and particularly to the hands and feet. In epidermodysplasia, they are often much more widely distributed and more polymorphic and may be pigmented. Both conditions are usually either present at birth or develop in infancy or at puberty, but epidermodysplasia is more liable than acrokeratosis to appear for the first time later in life. The conditions can be very clearly distinguished histologically by the presence of conspicuous vacuolation in epidermodysplasia. Some authorities believe this change is identical with that occurring in plane warts, but others consider that it is pathognomonic (Frühling and Bonjean, 1945). The published pedigrees of cases of epidermodysplasia show that it is inherited as a recessive character, whereas acrokeratosis is inherited as a dominant. The most important difference is that malignant transformation is not uncommon in epidermodysplasia and may even occur before the age of twenty, whereas it has not been recorded in acrokeratosis although some cases have been followed into old age.

Acrokeratosis may be present in Darier's disease, when it retains its usual histological features. In both Darier's disease and in acrokeratosis, finger-prints may demonstrate small breaks in the papillary ridges and small keratoses (Costa and Morais, 1949). There may be some genetic link between the two syndromes.

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Porokeratosis [Mibelli].—DR. STEPHEN GOLD.

A married woman aged 60. She has suffered for the past fifteen years from cracking and scaling of the lower lip and a gradually extending symmetrical change of the skin

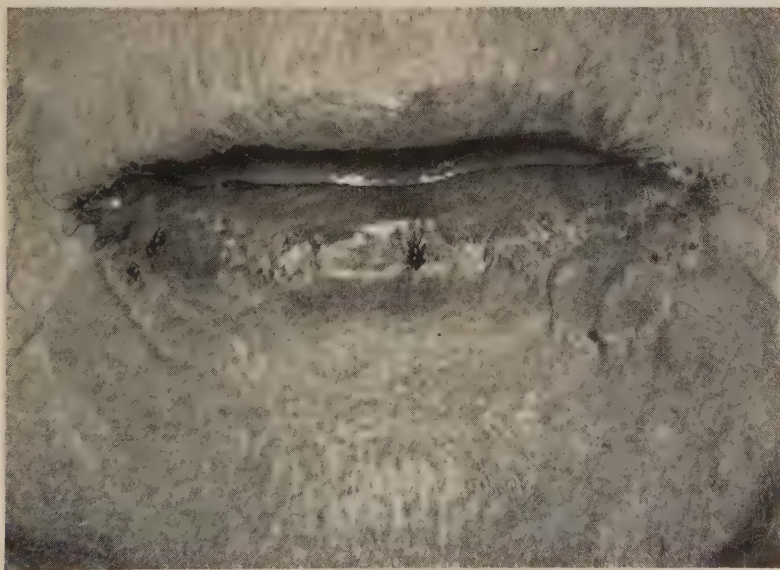


FIG. 1.

below the angles of the mouth. This has produced two small smooth atrophic areas on either side which are bounded by a clearly defined wall or ridge (Fig. 1). This ridge has the characteristic features of porokeratosis.

Investigations.—Blood W.R. and Kahn negative. Skin biopsy did not reveal any characteristic histological change.

Benign Mucous Membrane Pemphigoid.—DR. LOUIS FORMAN.

A married woman, aged 28.

History.—Blisters on the gingivae, gums, roof of the mouth and cheeks for 10 months. They relapse at different sites and some become confluent. Eight months ago, blisters appeared on the breasts and have relapsed, leaving a red, slightly atrophic patch.

Examination.—The gingivae and interdental papillae are red and eroded, or are covered by a layer of necrotic epithelium which can easily be removed; a small blister can be seen. There is evidence of blistering on the right cheek and the chest. She is seven months pregnant.

Histology (chest).—A sub-epidermal blister.

Comment.—The small tense blisters which do not rupture easily or spread with pressure are not those of pemphigus. Again, the recurrence of blisters in the same areas of the skin is typical of benign mucous membrane pemphigoid.

DISCUSSION.

DR. G. B. DOWLING : I have had no personal experience in treating these patients. Sneddon and Church in their article on the subject stated that treatment with steroids was almost completely ineffective.

DR. A. ROOK : In one case which I have treated in recent months there has been no response to cortisone.

DR. R. T. BRAIN : I have had two cases, both women, and cortisone did not affect them but ACTH did. I could always control the condition with ACTH but relapses occurred with domestic and emotional stress. I felt that the response was related to the patients' confidence. ACTH arouses them from their lethargic depression, and I think that a double factor is involved.

THE PRESIDENT : Lever believes that steroids are of value. My own experience in two elderly women with severe involvement of the mouth in one case and of the eyes in the other, is that response to prolonged high dosage of 300 mg. of cortisone a day, is unsatisfactory. One of these patients developed collapse of the spine as a complication of steroid therapy, which is therefore best avoided. I regard the disease as a localized dystrophic epidermolysis bullosa.

The following cases have been published in *Proc. R. Soc. Med.*, **50**, 473 :

Still's Disease with Pseudoxanthoma Elasticum.—DR. STEPHEN GOLD.

Xeroderma Pigmentosum.—DR. STEPHEN GOLD.

Xeroderma Pigmentosum.—DR. B. SCHWARTZ (for DR. HUGH GORDON).

Dermatomyositis.—DR. B. SCHWARTZ.

The following cases also were shown :

? **Neurofibroma.**—DR. PATRICK HALL-SMITH.

[1] **Necrobiosis Lipoidica**, [2] **Leuconychia Congenita**, [3] **Naevus of Ota**.
—DR. STEPHEN GOLD.

BRITISH ASSOCIATION OF DERMATOLOGY.

THIRTY-EIGHTH ANNUAL MEETING.

The 38th Annual Meeting of the Association will be held in Cardiff on 3, 4 and 5 July 1958 under the Presidency of Dr. J. H. Twiston Davies.

The main subject will be "Endocrine Aspects of Dermatology". Those wishing to contribute short papers should communicate with the local Hon. Secretary, Dr. E. Waddington.

OXFORD REGION DERMATOLOGICAL GROUP.

Aylesbury, 1 June 1957.

Cases shown by Dr. D. S. WILKINSON.

Lymphocytic Infiltration of the Skin with Secondary Anetoderma. Psoriasis.

A woman aged 35 years.

She was first seen two years ago with groups of lilac-pink, slightly infiltrated lesions around the shoulders and upper arms, the result, she believed, of having been gripped forcibly in the course of her work as a prison wardress. A biopsy at that time showed a fairly intense dermal infiltrate composed almost entirely of lymphocytes. No vascular changes were seen. Other investigations were normal.

In November 1956, when she was 20 weeks pregnant, she was found to have orthostatic albuminuria. A routine W.R. and Kahn were both positive in a dilution of 1/16, but later became negative. On a full investigation she was shown to have a negative Wasserman and P.P.R., but a positive Kahn reaction. This was thought to be non-treponemal. The T.P.I. reaction was negative. It was concluded there was no evidence of syphilitic infection on the serological tests.

When seen at the 38th week of pregnancy, she had developed an extreme degree of hyperkeratosis and discoloration of several finger nails. She also had urticaria. The patches on the shoulders had now become atrophic, of a faint lilac colour and with loose, baggy, overlying skin. They were no longer infiltrated and had not extended beyond their original confines.

Two weeks after birth the baby developed thrush. The mother's nail dystrophy increased and psoriatic patches appeared on the buttocks and hands. There was a monilial dermatitis of the vulva and thighs from which *C. albicans* was cultured.

On examination (three months after delivery) there has been a very considerable improvement in the nails which are rapidly becoming normal. The psoriatic patches have disappeared. No candida or trichophyton has been isolated from the nails.

Comment.—The anetoderma in this case does not fit in any of the classical patterns and appears to have followed exactly on the areas that had been the site of this intense lymphocytic infiltration. Whether this was traumatic or not is open to doubt, but the shape and distribution of the areas suggested it. The significance of the positive Kahn test is not known. The abrupt onset of psoriasis chiefly affecting the nails and subsequent regression after pregnancy are also of interest.

Subcorneal Pustular Dermatoses.

A woman aged 79 years.

One of the original cases described by Sneddon and Wilkinson. Since being shown at the Anglo-French Meeting in 1956 there has been little change in the condition, which has followed a course of exacerbations and spontaneous improvement. On the whole it has been better while she has been taking Dapsone but the effect of this drug has been progressively less marked. The pustules continue to be flaccid, subcorneal and sterile. Groups have appeared on the side of the neck. Her health has remained good.

The following cases also were shown :

Identical twins with Multiple Haemangiomas. Colloidon Baby, now five years old. **Keratoderma Palmare et Plantare.** "Tufted" Naevus of Scalp. **Necrobiosis Lipoidica Diabeticorum.** **Granulomatosis Disciformis** with Sarcoidosis. **Miliary Sarcoid.** **Multiple Leiomyomas.** Raynaud's Disease. **Purpuric Dermatitis?** Textile. **Poikiloderma Vasculare Atrophicum.** **Pityriasis Rubra Pilaris.** **Lichen Plano-pilaris.** **Urticaria Pigmentosa.** **Nodular Vasculitis.** **Reiter's Syndrome.**

CURRENT LITERATURE.

PATHOPHYSIOLOGY OF RINGWORM INFECTIONS IN ANIMALS WITH SKIN CYCLES. A. M. KLIGMAN. (1956) *J. invest. Derm.*, 27, 171.

Mice can be infected with ringworm only between the 12th and the 16th day of anagen: that is to say the odds are 7 to 1 against an animal being susceptible to random inoculation. The onset of telogen ends the infection so it can only last from 4 to 9 days. But there is no immunity, and subsequent infections run the same course. The author comments both on the present-day rarity of mouse "favus" and on the contrast between the insusceptibility to experimental infection and the high morbidity in some spontaneous epizootics.

Mice have 4 different kinds of hair in their coats—zigzags (lanugo undercoat), auchenes, monotrichs and awls. Ringworm attacks only the last two, growing in the comparatively shallow cortex and producing the appearance of an ectothrix infection. However violent the inflammatory reaction the follicle survives. J. H. T. D.

THE ANATOMY AND HISTOCHEMISTRY OF THE ARTERIOVENOUS ANASTOMOSIS IN HUMAN DIGITAL SKIN. J. G. RUKAVINA, W. D. BLOCK and A. C. CURTIS. (1956) *J. invest. Derm.*, 27, 133.

In contrast with other cutaneous vessels the *glomi* [sic] have cholinergic as well as adrenergic innervation and the smooth muscle stains metachromatically with toluidin blue.

A valuable and readable description of this elusive little organ.

J. H. T. D.

THE URINARY 17-KETOSTEROIDS IN ACNE VULGARIS BETWEEN 11 AND 13 YEARS OF AGE. F. RONCHESE and W. T. CARAWAY. (1956) *J. invest. Derm.*, 27, 147.

Same as in normal subjects of the same age.

J. H. T. D.

INTRADERMAL TEST IN AMERICAN LEISHMANIASIS WITH A POLYSACCHARIDE FRACTION ISOLATED FROM *L. BRAZILIENSIS*. T. A. FURTADO and J. PELLEGRINO. (1956) *J. invest. Derm.*, 27, 53.

A reliable skin test for allergy to *Leishmania* can be obtained by means of a complicated decoction of cultivated microbes consisting mainly of their specific polysaccharide.

J. H. T. D.

ADVANTAGES OF COMBINING HYDROCORTISONE AND OXYTETRACYCLINE TOPICALLY.

T. CORNBLEET, S. BARSKY and L. HOIT. (1956) *J. invest. Derm.*, 27, 61.

(An infallible portent of impending desuetude is the combination of the fashionable remedy with one that held the field last year.) But the authors, confident in the millenium, attribute the failure of many diseases to respond to their specific remedies to a multiplicity of pathogenesis. "More often an initial ailment predisposes and leads to another, or they become so closely associated or intertwined as to appear as one and to defy separation. Such is the case frequently with many kinds of alteration of the skin where it is possible to recognize the ordinary features of multiple specific dermatoses present side by side."

J. H. T. D.

STUDIES ON THE GROWTH OF BACTERIA IN THE HUMAN EAR CANAL. E. T. PERRY and A. C. NICHOLS. (1956) *J. invest. Derm.*, 27, 165.

The flora is much the same as that of the general cutaneous surface.

Cerumen has no bacteriostatic properties.

Pseudomonas aeruginosa ("*b. pyocyaneus*") failed to cause any mischief in the meatus of 7 healthy volunteers and after a week had disappeared.

J. H. T. D.

THE BACTERIA RESPONSIBLE FOR APOKRINE ODOUR. J. S. STRAUSS and A. M. KLIGMAN. (1956) *J. invest. Derm.*, 27, 67.

Not only the diphtheroids (which we all know make the same kind of nasty smell on the agar slope) but many cocci, coagulase positive or negative, protein and other microbes are capable of generating a powerful odour from a droplet of apocrine sweat otherwise not subject to decomposition.

J. H. T. D.

RESPIRATORY ACTIVITY AND NUCLEIC ACID CONTENT OF SOME TISSUES FROM GUINEA-PIGS SENSITIZED TO 2-4 DINITROCHLOROBENZENE. L. L. GERSHBEIN, B. K. KROTOZYSKI, M. J. BRUNNER and A. J. DOMNAS. (1956) *J. invest. Derm.*, **27**, 73.

Sensitization of skin, lymph-nodes, spleen and bone marrow does not affect its respiration even in the presence of the antigen. But skin in which an antigen-antibody reaction had already taken place took up more oxygen.

J. H. T. D.

ONYCHOMYCOSIS. AN EXPERIMENTAL STUDY. X. VILANOVA, M. CASANOVAS and J. FRANCINO. (1956) *J. invest. Derm.*, **27**, 77.

Out of 216 attempts to infect the nail or nail folds with various dermatophytes, lesions were obtained in only 52, all of them self-limiting within 180 days.

J. H. T. D.

THE EFFECT OF X-RAYS ON THE PHOSPHORUS CONTENT OF THE DESOXYRIBONUCLEIC ACID, RIBONUCLEIC ACID AND LIPOID FRACTIONS OF THE EPIDERMIS IN RATS. M. GARAZSI and I. DEME. (1956) *J. invest. Derm.*, **27**, 49.

During the 7 days following the application of 3000 r with a contact x-ray machine the phosphorus content of the DNA, RNA, and lipid of rat epidermis is progressively reduced.

J. H. T. D.

BENIGN MICROBIC LOCALISED GANGRENE OF TOURAINE. C. AGUILERA MARURI. (1957) *Actas dermo-sif., Madrid*, **48**, 168.

A healthy man aged 50 developed an ulcer with an adherent black slough on the internal aspect of the right buttock. There was no history of trauma or any abnormality of the skin. Three months later a similar lesion appeared on the part of the other buttock that was in direct contact with the original lesion.

G. W. B.

PRETIBIAL MYXOEDEMA. LOCAL ACTION OF HYDROCORTISONE ACETATE. P. A. VIGLIOGLIA and M. RAPAPORT. (1956) *Rev. Ass. med. Argentina*, **70**, 372.

The authors injected 0.2 ml. of a saline suspension daily for a month, and made biopsies weekly. Clinically the lesions turned from violet to pink and lost their infiltration. Histologically the oedema disappeared from the dermis as did the inflammatory changes, and the normal architecture of fibro-collagen tissue was restored.

G. W. B.

THE TREATMENT OF MULTIPLE SKIN ABSCESES IN INFANTS. F. MIEDZINSKI and Z. ANISIMOWICZ. (1957) *Derm. Wschr.*, **135**, 605.

Eighty cases of this condition which is known in the American literature as multiple sweat gland abscesses of infants are reviewed. The maximum incidence is in the first four months of life and during summer and autumn. There was a 5% mortality owing to the patients being admitted to hospital in a poor general condition. Mild cases responded well to topical and general measures. More severe cases required antibiotics and frequently blood transfusions. The organism was usually a staphylococcus aureus resistant to penicillin but as a rule sensitive to aureomycin which was given with good results.

W. G. T.

BLOOD LIPOIDS, LIPOPROTEINS AND PROTEINS IN PSORIASIS. J. RÁDL, Z. KRAUS and M. TOUŠEK. (1957) *Derm. Wschr.*, **135**, 609.

Abnormalities of metabolism in psoriasis have been reported on many occasions. The authors used modern methods of investigation to re-examine this question.

An increase of total lipaemia and of cholesterolaemia was observed together with a diminution of the esterification index. There is an increase of the β -fraction in the lipoprotein spectrum, the α and γ fractions being diminished. There was no abnormality of the protein metabolism. The cause of these abnormalities lies probably in the function of those organs, such as adrenals, pituitary and central nervous system, that control metabolism but a primary error of metabolism may also have to be considered.

W. G. T.

THE MICROBIOLOGY OF ONYCHOMYCOSSES. E. BALOGH. (1957) *Derm. Wschr.*, **135**, 618.

In the course of about a year 228 cases of this condition were seen. Examination for fungi was positive in all. In 148 cases cultures were positive: 38 cases produced epidermophyton, one of them

Epidermophyton inguinale, associated with an infection of the soles of the feet. 12.7% of cases showed scopulariopsis and penicillium was grown in 22 cases. The author thinks the latter is to be considered as a saprophyte that easily grows on a nail previously damaged by epidermophyton infection.

W. G. T.

MOLLUSCUM PSEUDOCARCINOMATOSUM AND CARCINOMA. H. FLEGEL. (1957) *Derm. Wschr.*, **135**, 153.

A typical case of molluscum sebaceum was treated with x-rays in 1953. Three years later there was a recurrence with the histology of an epithelioma. Malignant degeneration of molluscum sebaceum has been reported on a number of occasions. Histology does not always help in the differential diagnosis and only the course proves the eventual diagnosis. Molluscum sebaceum is a border line condition between benign and malignant growth, and growth-controlling factors determine whether the condition remains self limited or whether irregular growth supervenes.

W. G. T.

THE INDICATIONS FOR PYREXIAL THERAPY IN NEURODERMATITIS. L. MÜLLER. (1957) *Derm. Wschr.*, **135**, 156.

One hundred and ten cases of neurodermatitis were treated with pyriferylene. The average duration of treatment was about 20 days. Only cases that had resisted all other forms of treatment were subjected to this therapy. The ages varied between 15 and 46 years. Three cases of recurrence became known afterwards. The treatment is entirely symptomatic and no influence on the cause of the condition is claimed. The fever makes such demands on the patient that previously active factors, particularly psychogenic ones, are pushed into the background. Local treatment was unavoidable in some cases and was thought to be required to facilitate local resorption and removal of breakdown products.

W. G. T.

HEBERDEN'S NODES. G. WEBER. (1957) *Derm. Wschr.*, **135**, 162.

This condition, first described by Heberden over 150 years ago, has been re-examined in recent years by Stecher and his collaborators. It depends on an osteoarthritis of the fingers and radiologically spur formation is found. The nodes, which are painful, usually occur over the distal interphalangeal joints of the 2nd, 3rd and 5th fingers, less frequently over the 2nd and 4th proximal joints. The condition is either idiopathic or traumatic. The idiopathic form is much more common in women and dominant, whereas it is recessive in men. The traumatic form is more common in men. Differential diagnosis from gout, rheumatoid arthritis and rheumatic nodules is easy.

W. G. T.

COMBINED ANTIHISTAMINE AND HYDROCORTISONE OINTMENTS IN DERMATOLOGY. W. H. WEYER. (1957) *Derm. Wschr.*, **135**, 179.

This combined local treatment has been used in 225 cases of eczematous dermatoses and was found to be very satisfactory. It was possible to reduce hydrocortisone to 0.4 and 0.5% which resulted in great economy. The antihistamine used was 1% Ilvin made by Merck. The combination of the anti-allergic anti-histamine and the anti-inflammatory steroid was considered to be equal and in some cases superior in therapeutic action to 1% hydrocortisone ointment.

W. G. T.

BULLOUS DERMATITIS DUE TO WALNUT PEEL. R. BARNISKE. (1957) *Derm. Wschr.*, **135**, 189.

The condition was first described by Siegel in 1954. His patient developed the eruption 2 days after first contact with green walnuts. The author's patient developed the eruption during the third season in which she had handled and peeled the nuts. The sensitising agent according to Siegel is juglandic acid, an α -naphthoquinone derivative.

W. G. T.

THE ATTRIBUTABILITY OF DERMATOSES TO MILITARY SERVICE. H. A. GOTTRON. (1957) *Berufsdermatosen*, **5**, 1.

In the course of his paper the question of the attributability of certain rarer dermatoses such as cold damage, scleroderma, lupus erythematosus, scleredema, acrodermatitis atrophicans, pemphigus vulgaris and dermatitis herpetiformis and some less rare ones as urticaria, acne con-

globata and skin carcinoma is examined. The difficulties confronting the dermatologist in deciding this question and the importance of taking into consideration all possible evidence are stressed. Most of these conditions can under certain circumstances be found to be due to war service.

W. G. T.

THE LIABILITY OF WORKING WOMEN TO INDUSTRIAL DERMATOSES. H. GARTMANN. (1957) *Berufsdermatosen*, 5, 23.

The higher incidence of industrial dermatoses in women is frequently reported in the literature. Apart from the possibility of an increased hazard during menstrual periods and pregnancy and the added exposure of women to irritants in the home the contention that women are more liable to dermatoses is dismissed and limited statistical evidence derived from 282 men and 190 women suffering from eczematous dermatitis of the exposed parts is quoted in support. The variations obtained were without statistical significance.

W. G. T.

OCCUPATIONAL SKIN CANCER. A. TOURAINE. (1957) *Berufsdermatosen*, 5, 49.

The existence of occupational skin cancer both secondary to trauma of various kinds and due to the action of various influences encountered occupationally has been proved for some time. The occurrence of such cases is probably rarer than could be assumed from the wealth of publications on the subject. The theory of cocarcinogenesis, demanding the simultaneous occurrence in the same patient of exogenous and endogenous, including hereditary, factors is considered to be of increasing importance. Each case has to be judged on its merits and doubtful cases must be decided in favour of the patient. Strict medical supervision of all occupations involving the risk of skin cancer is advocated.

W. G. T.

OCCUPATIONAL DERMATITIS IN THE CINEMATOGRAPHIC INDUSTRY. P. POPCHRISTOV, N. BALEVSKA and P. MICHAJLOV. (1957) *Berufsdermatosen*, 5, 70.

A report of 40 cases of industrial disease, both general and affecting the skin, in workers in the film producing industry. The commonest causes were a colour film developer containing 1-diethylamine-4-aminobenzol-sulphate and a "cement" containing acetone. Other causes were acids, amyl acetate and black and white film developers.

A number of recommendations are made for diminishing the high incidence of occupational disease in this industry. Most measures are of a social nature but prophylactic examination of workers, skin testing of new workers and early removal of sensitized personnel are suggestions of interest to the dermatologist.

W. G. T.

OCCUPATIONAL DERMATOSES CAUSED BY COLD SETTING ETHOXYLENE RESINS (EPOXIDE RESINS). E. GRANDJEAN. (1957) *Berufsdermatosen*, 5, 97.

Araldite is a cold setting resin which is widely used in industry. Dermatoses can be caused either by the liquid resin, the hardener used with it (triethylenetetramine) or the mixture of the two before it has properly set. Eleven industrial undertakings in 4 different countries were examined and of the 328 workers handling the substance more than half had suffered from dermatoses. Contact is the main cause of skin eruptions, though vapours may cause them. The number of cases could however be reduced considerably if contact was strictly avoided and when comparing the 11 factories investigated it is obvious that the incidence is lowest where protective and hygienic measures are best developed.

W. G. T.

TOPICAL STEROID THERAPY IN OCCUPATIONAL DERMATOSES. H. M. ROBINSON, JR. (1957) *Berufsdermatosen*, 5, 116.

■ Dermatoses now represent 60% of all industrial disease in the U.S.A. The success of topical steroid therapy in various skin conditions has led to its application to cases of occupational dermatoses and this has been extremely successful. Five case histories are quoted to illustrate this. The preparations used were hydrocortisone diethylamino-acetate-hydrochloride, prednisolone diethylamino-acetate-hydrochloride and a mixture of hydrocortisone diethylamino-acetate and neomycin. It was found that 0.5% hydrocortisone-diethylamino-acetate-hydrochloride and 0.25% prednisolone diethylamino-acetate-hydrochloride were as effective as 1% hydrocortisone as free alcohol.

W. G. T.

MODERN ANTIBACTERIAL AND ANTIMYCOTIC DISINFECTION OF MINERS' WASH-ROOMS.K. A. PRIMAVESI. (1957) *Berufsdermatosen*, 5, 123.

Any disinfectant used must have a good bactericidal effect, a broad spectrum and a good fungicidal action, it must be safe in the concentration recommended and cheap. Cleanliness is of first importance. Floors should be scrubbed with a combination of soap and disinfectant and the walls should be sprayed with disinfectant. Materials not easily cleansed should be avoided in furnishing wash-rooms; rubber foot wear with anti-fungal properties is recommended.

W. G. T.

THE SIGNIFICANCE OF FOCAL PROCESSES IN OCCUPATIONAL DERMATOSES. H. WILDE.(1957) *Berufsdermatosen*, 5, 130.

It is stated that focal processes such as tinea interdigitalis are of greatest importance in industrial dermatoses. They make the skin more sensitive to external irritants and the treatment of the developed condition more difficult.

W. G. T.

A CASE OF CALCINOSIS CUTIS. C. SABATINI and R. TAGLIAVINI. (1957) *Arch. ital. Derm. Sif.*, 28, 286.

The case and the classification of calcinosis are considered from the biochemical standpoint.

A. L.

A CASE OF HERPES ZOSTER LOCALIZED EXCLUSIVELY TO THE ARM. C. GIACOMETTI.(1957) *Arch. ital. Derm. Sif.*, 28, 299.

Restriction of the eruption of zoster to a limb without involvement of the trunk is said to be rare. In the case reported unilateral neuralgia referable to many nerve roots was followed by an eruption localized to that part of the second thoracic segment which supplies the arm, and the pain was intensified and concentrated in this spot. The rapid recovery was attributed to injections of a preparation of hog's stomach.

A. L.

RESEARCHES ON THE POSSIBILITY OF INHIBITION OF THE MIDDLEBROOK-DUBOS REACTION IN THE SERA OF LEPERS BY MEANS OF ABSORPTION WITH MARIANIN AND TUBERCULIN. S. ZOCCHI and G. FARRIS. (1957) *Arch. ital. Derm. Sif.*, 28, 307.

Marianin, which is produced from *Mycobacterium marianum*, failed to inhibit the reaction whereas tuberculin and the Middlebrook-Dubos antigen did so.

A. L.

RECURRENT APHTHOUS ULCERATION OF THE MOUTH. W. SIRCUS, R. CHURCH and J.KELLEHER. (1957) *Quart. J. Med.*, N.S., 26, 235.

One in five of the population suffers, at some period in their life, from this condition. It is somewhat more common in females. Onset is usually in the second decade, but in 10% of females the first attack occurred between the ages of 50 and 59 whereas no ulcers began in men in that age group. There is a rhythmical periodicity in the attacks in most subjects. Mental stress was an outstanding feature in precipitating attacks being found in 21% of patients.

There appeared to be no associated conditions in the patients examined, even dyspepsia being no more common than in the average population.

Controlled therapeutic trials with many substances showed only the benefit of local aureomycin in reducing the duration of an average attack from ten to five days.

Extensive virus and serological studies were carried out: the results were somewhat inconclusive.

This is an important article containing much useful factual information.

J. M. B.

DEATHS ASSOCIATED WITH STEROID HORMONE THERAPY. J. D. ALLANBY. (1957)*Lancet*, i, 1104.

Eighteen deaths occurring in over 400 patients treated with steroid hormones are analysed. Of these 14 were directly or in part due to steroid therapy. Infection accounted for 6 deaths, gastro-intestinal perforation for 2 and gastro-intestinal haemorrhage for 3, the remaining deaths being due to congestive cardiac failure, hypersensitivity to corticotropin and post-operative adrenal failure. The danger of adrenal failure occurring in cortisone treated patients exposed to additional stress such as an operation or an infection is discussed and it is suggested that such

patients should receive an increased dose of steroid hormone rather than the withdrawal of such treatment.

R. H. M.

POST-OPERATIVE COLLAPSE DUE TO ADRENAL INSUFFICIENCY. G. SLANEY and B. N. BROOKE. (1957) *Lancet*, i, 1167.

Post-operative collapse occurred in 7 patients who had been treated with cortisone for a period before operation. Four of the patients died and the authors consider that adrenal insufficiency induced by previous cortisone therapy was the cause. They describe a scheme of cortisone and corticotropin therapy to be given to patients undergoing operations who have had corticosteroid therapy during the previous year.

R. H. M.

THE EFFECT ON SERUM CHOLESTEROL OF DIETS CONTAINING DIFFERENT FATS. H. MALMROSE and G. WIGAND. (1957) *Lancet*, ii, 1.

When fats, particularly corn oil, containing poly-unsaturated fatty acids were added to the diet of healthy subjects the serum cholesterol level fell. This also happened when patients with essential hypercholesterolaemia were given a diet rich in corn oil and artificial dairy products made with corn oil. Xanthomata did not show any regression even in those patients who had had the corn oil diet for over a year.

R. H. M.

THE INFLUENCE OF IONIZING RADIATION ON THE REACTIVITY OF THE SKIN TO PYOGENIC INFECTIONS AND SOME EXTERNAL IRRITANTS. V. I. SAMTZOVA. (1956) *Vestnik Ven. i Derm. Moscow*, 4, 3.

Rabbits were subjected to general irradiation with x-rays (750 r), a dose sufficient to cause irradiation sickness, leukopenia, etc. The skin of such animals developed an intense haemorrhagic reaction to chemical irritations; and to infection with pyogenic organisms (besides a necrotic local pyoderma) a general reaction sometimes fatal. The response to ultraviolet light (Kromayer lamp) varied in some there was increased tolerance, due it is suggested to depression of the central nervous system, as increased tolerance to ultra-violet light has been reported during ether narcosis and spinal anaesthesia.

M. S. S.

THE INFLUENCE OF COBALT ON THE ACTIVITY OF PENICILLIN. N. M. OVCHINNIKOV and K. S. KUTUKOVA. (1956) *Vestnik Ven. i Derm. Moscow*, 6, 34.

The authors find that penicillin by injection followed by an injection of chloride or carbonate of cobalt is more effective than penicillin alone in the treatment of the syphilitic chancre in experimental rabbits (e.g. spirochaetes disappear more rapidly). They have not found the enhancing effect of the cobalt quite so great as that reported by other authors, but this they attribute to their choice of infection, the spirochaete rather than, for example, the staphylococcus.

M. S. S.

SARCOIDOSIS AND PREGNANCY. R. L. MAYCOCK, R. D. SULLIVAN, R. G. GREENING and R. JONES. (1957) *J. Amer. med. Ass.*, 164, 158.

The course of 16 pregnancies was observed in 10 patients with sarcoidosis. In 8 of the patients there was some improvement in the manifestations of the disease during pregnancy. Relapse frequently occurred after delivery. There were two premature deliveries and one stillbirth, and three congenital abnormalities. The apparent beneficial effect of pregnancy may be an additional argument against the tuberculous origin of the disease.

A. J. R.

CUTANEOUS EFFECTS OF SOAPS AND SYNTHETIC DETERGENTS. R. R. SUSKIND. (1957) *J. Amer. med. Ass.*, 163, 943.

In this report to the Committee on Cosmetics of the A.M.A. the difficulty of assessing clinically the cutaneous effects of detergents is emphasized. It is probable that the action of several factors in combination is necessary to induce housewives' dermatitis. The author carried out an investigation to confirm a report that immersion in detergent solution produced no significant changes in dermatitis of the hands. One hand of 45 hospitalized patients was exposed for 30 minutes twice daily to two heavy-duty cleaning agents, the other hand serving as a control. In no case did the dermatitis of the test hand become worse.

A. J. R.

DIAGNOSIS AND TREATMENT OF VESICULAR ERUPTIONS OF THE HANDS. S. A. M. JOHNSON. (1957) *J. Amer. med. Ass.*, **163**, 1106.

This review presents a systematic account of the vesicular eruptions of the hands but incorporates no new facts. Many of the conventional opinions here repeated still lack scientific confirmation.

A. J. R.

ACTION OF EMOLLIENT CREAMS AND THEIR ADDITIVES. I. H. BLANK. (1957) *J. Amer. med. Ass.*, **164**, 412.

"Most emollients are a mixture of an oil and water. Only water can keep the horny layer flexible and most of the water in the emulsions rapidly evaporates. The oil retards the evaporation of water from the cutaneous surface and may also relieve the symptoms of dryness. There is little evidence that the external application of vitamin A corrects abnormal keratinization and it has yet to be proved that oestrogen creams are of benefit to the ageing skin.

A. J. R.

THE NATURAL HISTORY OF HERPES ZOSTER. C. F. BURGOON, J. S. BURGOON and G. D. BALDRIDGE. (1957) *J. Amer. med. Ass.*, **164**, 265.

The analysis of the records of 206 patients with herpes zoster showed that the incidence of the disease was not influenced by sex, race or season. Correlation of age incidence with population distribution shows an increased incidence over 60. The skin lesions are more severe and post-herpetic neuralgia is more common in the older patient. Ocular complications appeared not to be related to the ageing process.

A. J. R.

CLINICAL APPRAISAL OF DERMATOSES DUE TO COSMETICS. C. T. NELSON. (1957) *J. Amer. med. Ass.*, **163**, 740.

This is the first of a series of papers on cosmetics, and is concerned with general principles. The incidence of dermatitis caused by cosmetics cannot be reliably estimated as many cases never reach dermatologists. The paramount importance of the history in diagnosis is emphasized. The author believes that patch-testing can be expected to confirm the diagnosis in no more than 30 to 35% of cases.

A. J. R.

PLASMOCYTOSIS AND CRYOGLOBULINEMIA IN CANCER. M. G. BOHRD. (1957) *J. Amer. med. Ass.*, **164**, 18.

A woman aged 68, with a small carcinoma of the breast, was found to have a marked plasmocytosis of peripheral blood and bone marrow. She also had cryoglobulinaemia manifest as urticaria present only in the mornings and induced by the application of ice to the skin. The cryoglobulinaemia disappeared a few weeks after mastectomy and the plasmocytosis had disappeared even before operation. The relationship of the plasmocytosis and cryoglobulinaemia to the immune process in cancer is discussed.

A. J. R.

GIN AND TONIC—A CAUSE OF DERMATITIS. F. G. NOVY and G. R. LAMB. (1957) *J. Amer. med. Ass.*, **164**, 91.

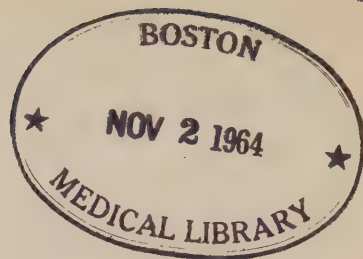
Tonic-water may contain as much as 30 mg. of quinine per pint. Quinine sensitivity is not rare. Tinnitus, headaches, fever and gastrointestinal symptoms may occur alone or with various skin lesions, erythematous, papular or bullous. A severe reaction is described in a man aged 36 who had consumed about 45 mg. of quinine in "gin and tonics" in 3 hours.

A. J. R.

USE OF PREDNISONE AND PREDNISOLONE IN TREATMENT OF ALLERGIC DISEASES. E. B. BROWN and T. SEIDEMAN. (1957) *J. Amer. med. Ass.*, **163**, 713.

The author confirms the value of prednisone in shortening the course of the self-limiting allergic conditions. He also emphasizes the value of prednisone or prednisolone in selected cases of asthma, and of seasonal or perennial rhinitis. Over 60% of 64 asthmatics received 90–100% relief while receiving treatment and 90% of 10 patients with perennial rhinitis were similarly relieved. Side-reactions were observed in 33 of 190 patients; increased appetite, urinary frequency and insomnia were the commonest.

A. J. R.



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